Myocardial scar Quantified by Selvester score and correlation with MRI in Hypertrophic cardiomyopathy(HCM) patients

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CERTIFICATE

This is to certify that the work incorporated in this thesis titled "**Myocardial scar Quantified by Selvester score and correlation with MRI in Hypertrophic cardiomyopathy(HCM) patients**" for the degree of DM CARDIOVASCULAR IMAGING AND VASCULAR INTERVENTIONAL RADIOLOGY has been carried out by Dr.Divyesh Dadhania under our supervision and guidance. The work done in connection with this thesis has been carried out by the candidate himself and is genuine.

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Abstract

Objectives: To test the hypothesis that modified Selvester score obtained by 12 lead ECG quantifies myocardial scar and correlates with CMR LGE techniques in Hypertrophic cardiomyopathy patients.

Background: HCM is a most common genetic cardiomyopathy which has heterogeneous phenotypic expression. It is one of the common cause of sudden cardiac death in young adults Various strategies exists to stratify HCM patients into high risk vs low risk for SCD.LGE by cardiac magnetic resonance is the gold-standard technique for detecting and quantifying myocardial scar which is considered and independent risk factor for future events in HCM patients. Considering the future risk of SCD and limited availability of CMR especially in developing countries, there is a need for a widely available screening method to measure scar burden in these patients. Twelve-lead electrocardiography (ECG) is inexpensive and universally available and can be readily used for Modified Selvester QRS scoring, which estimates scar size. This study aimed to establish the relation between ECG scar quantification and myocardial fibrosis (extent of myocardial delayed enhancement) measured by LGE CMR in HCM cohort.

Methods: This is an analytical cross sectional study. Seventy patients (n=70) with clinical and Echocardiographic diagnosis of HCM underwent a CMR examination with GBCA. LGE volume was quantified using the 2 techniques, +5SD and FWHM.12 lead ECG was analysed for modified Selvester score after identifying confounding factors (LBBB, RBBB, RBBB+LAFB, LVH, LAFB or No Confounder).Pearson correlation calculated between ECG Scar and CMR scar.

Results : Mean age of study cohort was 49.7 years (Range-19 to 71 years, M=53).Mean scar percentage by 5SD, FWHM and Selvester score was 9.3%, 10.3% and 9.2% respectively. Modified QRS score strongly correlated directly with 5SD (r=0.813,P-0.0005) and FWHM (r=0.751,P=0.0005) CMR-LGE. Diagnostic ability of QRS score to detect ≥1% scar showed high sensitivity in comparison to 5SD(Sensitivity-96.43%,Specificity-50%) and FWHM(Sensitivity-98.04%,Specificity-42.11).One way ANOVA test suggest there is no statistically significant difference among the mean scar quantification by 3 methods(F stat-0.29,p=0.7486).Bland Altman analysis suggest good agreement with only few observations lie outside 1.96SD range without

consistent bias of any method. Sub data analysis suggest that patients with NSVT on Holter study had higher scar burden by all 3 methods ($p< 0.005$) in comparison to patients with Normal Holter study. This suggest scar act as substrate for arrhythmogenesis. Another sub analysis suggest that LV scar burden has no impact in presence or absence of LVOT obstruction.

Conclusions: The Selvester QRS score facilitates quantitative measurement of the fibrotic burden in patients with HCM, and its findings were correlated strongly with those of LGE CMR methods. The inexpensive and widely available 12-lead ECG could potentially be used as a screening tool to quantify scar and identify high risk subgroup of HCM patients. It can be used alternatively when CMR is contraindicated or not available as well as during clinical follow up. These findings have implications for future investigations of QRS score in relation to risk stratification and clinical outcomes in HCM, including sudden cardiac death.

CONTENTS

ABBREVIATIONS

AHA	American heart association
CMR	Cardiac magnetic resonance
T	Tesla
GBCA	Gadolinium based contrast agent
LV	Left ventricle
LVH	Left ventricular hypertrophy
LVEF	Left ventricle ejection fraction
HCM	Hypertrophic cardiomyopathy
ASH	Asymmetric septal hypertrophy
HOCM	Hypertrophic obstructive cardiomyopathy
LVOTO	Left ventricular outflow tract obstruction
SPGR	Spoiled gradient recalled echo
CNR	Contrast noise ratio
SNR	Signal noise ratio
ECG	Electrocardiography
SAM	Systolic anterior motion
MR	Mitral regurgitation
LGE	Late gadolinium enhancement
b-SSFP	Balanced Steady state free precession
True FISP	Fast imaging with steady-state free precession
Balance FFE	Fast field echo
RBBB	Right bundle branch block
LBBB	Left bundle branch block
LAFB	Left anterior fascicular block
NYHA	New York heart association
PACS	Picture archiving and communication system
NSVT	Non sustained ventricular tachycardia
NT Pro BNP	N-terminal pro B type natriuretic peptide
FLASH	Fast low angle turbo shot
IR	Inversion recovery
PSIR	Phase sensitive inversion recovery
FIESTA	Fast imaging steady state acquisition
5SD	5 standard deviation
FWHM	Full width half maximum
MYH7	Myosin Heavy Chain7
MYBPC3	Myosin binding protein C3
SCD	Sudden cardiac death

AF	Atrial fibrillation
ICD	Intra-cardiac defibrillator
CRT	Cardiac resynchronization therapy
ECV	Extra cellular volume

INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is an autosomal dominant (AD) inherited disorder involving cardiac muscle with phenotypic expression to be about 0.2% (i.e., 1:500) in the general population (1). It is characterized by cardiac hypertrophy, unexplained by loading conditions with a nondilated left ventricle and normal or increased ejection fraction (2). HCM is caused by over 1400 mutations in at least 11 genes encoding proteins of the cardiac sarcomere resulting in dysfunction of the myocardium. Wide genetic heterogeneity of HCM manifest itself with wide variations in the morphologic expression of the disease like asymmetric septal hypertrophy (ASH-most common phenotypic variant), isolated mid-ventricular/apical, RV involvement and posteroseptal and isolated lateral wall hypertrophy. It is commonly diagnosed by Echocardiography by asymmetric septal hypertrophy with a maximum thickness of 15 mm or more (3). It is usually a diagnosis of exclusion, while other etiologies of LV hypertrophy including hypertension, valvular heart diseases and infiltrative cardiomyopathies needs to be ruled out. It is the most common cause of sudden cardiac death in less than 35 years and thus require adequate screening methods to detect the sudden cardiac death (SCD) risk. SCD in HCM patients is attributed to multiple factors of which one of the factor is ventricular arrhythmia due to myocardial scar. Evidence has shown a good correlation between the scar burden and the risk of SCD, independent of conventional risk factors (4, 5).

Currently CMR LGE has been established standard for scar detection and quantification related to various cardiac pathologies. Considering the future risk of SCD and limited availability of CMR especially in developing countries, there is a need for a widely available screening method to measure scar burden in these patients. Electrocardiographic techniques, i.e., 12-lead electrocardiography (ECG) and 24-hour Holter monitoring, have been used for years in this group of patients to detect Q wave (Suggestive of presence of scar) and NSVT. Selvester et al. has developed an objective and reproducible QRS score based on amplitude and duration of QRS complex in 12 lead ECG which can quantify fibrosis mainly in ischemic cardiomyopathy group of patients. However it is unusable in presence of multiple confounding factors which limits its widespread clinical utility. In 2009, Selvester scoring system was modified to use QRS scoring system in presence of confounding factors for fibrosis quantification. A few studies have compared scar burden determined by QRS score by ECG and Late gadolinium enhancement by CMR in ischemic cardiomyopathy with good correlation. However there is sparse literature regarding utility of Selvester score to estimate scar burden in HCM patients. This study aims to correlate scar burden measured by Selvester score with scar burden measured using CMR LGE techniques.

AIMS AND OBJECTIVES

Primary objective: To compare scar quantification done by Selvester QRS score of electrocardiography (ECG) with Cardiac MRI late gadolinium enhancement techniques.

Secondary objectives:

- To compare 5SD and FWHM methods in CMR for scar quantification by semi-automated tool.
- Effect of NSVT in relation to fibrosis in HCM patients.
- Ability of Selvester score to detect scar and to identify patients with high risk scar burden.
- To propose a MR corrected Selvester scar scoring system to improve the accuracy of the modified Selvester scoring for screening of hypertrophic cardiomyopathy patients

Null hypothesis: There is no significant difference among 3 methods for scar quantification in HCM patients (5SD, FWHM and Selvester score).

Alternate hypothesis: There is significant difference among 3 methods for scar quantification in HCM patients (5SD, FWHM and Selvester score).

REVIEW OF LITERATURE

Epidemiology

HCM is the most common genetic cardiomyopathy which is estimated to be 35 times common than other genetic cardiovascular diseases. Developed countries have reported incidence of 1 in 500 cases in general population attributable to robust medical systems and improved genetic detection facilities (6,7,8). However limited epidemiological data exists in developing countries including India due to the lack of adequate facilities for detection of the disease, poor screening programme and awareness among the population. Limited number of tertiary centres with expertise related to this condition is also a hindering factor for diagnosis and treatment of this disease. Recent analysis suggests that HCM is more common than previously estimated with the prevalence of HCM gene carriers estimated to be 1 in 200 people (2.5-fold more common than reported(9). This increasing prevalence of HCM has been attributed to the detection of new genetic mutations that encode the proteins of cardiac sarcomere chain and myosin-binding protein C.

Clinical definition

In HCM, morphologic expression is confined solely to the heart which is characterized predominantly by Left ventricular hypertrophy (LVH).This LVH should be in the absence of other cardiac, systemic, or metabolic disease capable of producing the magnitude of hypertrophy evident in a given patient and for which a disease-causing sarcomere (or sarcomere-related) variant is identified, or genetic aetiology remains unresolved (9). Diagnosis of HCM can be made using imaging (Echo or CMR) showing a maximal end-diastolic wall thickness ≥15 mm anywhere in the left ventricle, in the absence of another cause of hypertrophy in adults. Borderline hypertrophy of 13-14 mm can be diagnostic if family history of HCM is present or in case of positive genetic test. For the paediatric population a threshold of z >2.5 SD may be appropriate to identify early HCM in asymptomatic children with no family history, whereas for children with a definitive family history or a positive genetic test, a threshold of z >2 SD may be sufficient for early diagnosis (9).

Etiology:

HCM has been regarded as a monogenic cardiac disease, helping to consolidate a clinically heterogeneous disease into a single entity based on genetic substrate. Currently, 8 or more genes encoding proteins of the cardiac sarcomere or sarcomere-related structures have been implicated in

causing LVH. Approximately 30-60% of HCM patients have an identifiable genetic variant (9). Patients without any detectable genetic mutation suggest that other novel pathophysiologic mechanisms may be responsible or contribute to phenotypic expression in these affected patients with HCM. Beta myosin heavy chain 7 (MYH7) and myosin-binding protein C3 (MYBPC3) are two most commonly identified genetic mutation amongst genetically positive patients. Other genes (TNNI3, TNNT2, TPM1, MYL2, MYL3, ACTC1) account for a small proportion of patients (1% to 5%).The precise mechanisms by which genotypic mutation result in the clinical phenotype have not been fully elucidated. Mutant sarcomere genes trigger myocardial changes, leading to hypertrophy and fibrosis, which ultimately results in a stiff ventricle with systolic and diastolic dysfunction despite a preserved left ventricular ejection fraction (LVEF). Abnormal sarcomeric proteins may not be solely attributable for all clinical manifestations of HCM. Other features including abnormal intramural coronary arteries responsible for small vessel ischemia, elongated mitral valve leaflets, and congenital anomalies of the sub-mitral valve apparatus, which are widely recognized components of the HCM phenotype, appear to have no known direct association with sarcomere variants (9).

Pathogenesis

A wide array of mechanisms are implicated in the pathogenesis of HCM which can be categorised into 4 sets of interdependent mechanisms. The primary defect is the mutation.

1) Initial or proximal phenotypes: Due to direct effects of the mutations on the structure and function of the sarcomere proteins.
2) The intermediary or secondary phenotypes: Related to molecular changes due to changes in the sarcomere protein structure and function.
3) The tertiary(Histological) effects: Consequence of perturbation of a multiple molecular events in the myocardium, such as activation of the hypertrophic signalling pathways
4) Quaternary effects: Clinical presentation of HCM like LVOT obstruction, arrhythmias or heart failure.

It is important to differentiate the HCM induced by sarcomere protein mutation from the phenocopy conditions, later resulting from the storage of material inducing functional defects in myocytes causing impaired contraction (10,11).

Pathological changes in the myocardium

A) Macroscopic phenotype:

Left ventricular hypertrophy (LVH):

Asymmetric septal hypertrophy (ASH) is most common phenotypic expression, however apical and mid cavity involvement of the left ventricle have also been described. Basal anterior septum in continuity with the anterior free wall is the most common location for LVH.>15 mm LV wall thickness is considered diagnostic cut off for HCM. Previous studies have shown an average wall thickness of 21-22 mm in HCM cases and can reach a thickness of 50 mm. A maximum wall thickness of over 30 mm is associated with increased risk of sudden cardiac death (5,12). In HCM the left ventricular cavity is typically small, however, a dilated ventricle may be present in cases with progressive disease.

Left Ventricular Outflow Tract Obstruction (LVOTO)

Dynamic LVOTO is present in up to 75% of HCM case either at rest or with provocation (13).

Two mechanisms are described for LVOTO

1) Thickened basal septum causes narrowing of LVOT resulting into abnormal blood flow vectors which dynamically displace the mitral valve leaflets anteriorly
2) Altered anatomy of mitral valve apparatus like longer leaflets, anterior displacement of papillary muscles & mitral valve apparatus which resulting into abnormal flow vectors by venture effect and systolic anterior motion of mitral leaflets and causing LVOTO (14-17).

Increased LV systolic pressure due to LVOTO may contribute to LVH, myocardial ischemia, impaired relaxation, reduced stroke volume and heart failure. Peak LVOT gradient at rest ≥30 mm hg or ≥60 mm hg after provocation (with low or absent peak resting gradient) is suggestive of obstruction. Resting or provoked gradient ≥50 mm hg obstruction is considered to be threshold for septal reduction therapy in patients with drug refractory symptoms (2). Increased myocardial contractility, decreased preload/afterload will increase the LVOT gradient. LVOTO is usually diagnosed by Echo or CMR. If echocardiographic findings and clinical findings are discordant, invasive pressure measurement is indicated.

Myocardial scarring

Myocardial fibrosis is present in in up to 80 % of the HCM patients. CMR imaging with late gadolinium-enhancement (LGE) can be used to detect and quantify myocardial fibrosis and scarring. Moon et al. and Iles et al. demonstrated a significant relationship between histological collagen and the extent of LGE; myocardial segments containing >15% collagen were more likely to display LGE (18). Clinical observations have revealed that rather than being confined to the septum, the location of LGE fibrosis follows the pattern of LVH morphology. However, LGE is

not specific to HCM and can be seen in any case with the remodelling of the left ventricle. Previous studies have pointed towards the association of LGE to disease progression and sudden death (5). Ismail et al. studied over 700 patient and found that the amount of LGE was directly related to sudden cardiac death (19).

Diastolic dysfunction

Impaired relaxation occurs due to myocardial hypertrophy, ischemia, and replacement or interstitial fibrosis, delayed inactivation from abnormal intracellular calcium reuptake, high intracavitary pressures. With impairment in ventricular myocardial relaxation, greater dependency on the atrial systole for ventricular filling may occur, leading to poor tolerance of AF or similar arrhythmias in some patients (9).

Mitral regurgitation

Primary MR occurs due to abnormality in mitral leaflets. Secondary MR occurs due to severe LVOTO which causes SAM of mitral valve and malcoaptation of mitral leaflets as well as elevated intracavitary pressure. A posteriorly directed jet of MR in obstructive HCM correlates with SAM of the mitral valve. However anterior or central jet may also occur due to SAM (20). Severe MR may result into atrial dilatation and fibrosis which may lead to atrial arrhythmias.

Myocardial ischemia:

HCM patients are susceptible for MI due to mismatch between demand and supply. Studies showed that Myocardial hypertrophy, microvascular dysfunction with impaired coronary flow reserve, and medial hypertrophy of the intramural arterioles and their reduced density are common findings in HCM patients (21,22).These abnormalities are accentuated by the presence of hyper dynamic systolic function and LVOTO with high intracavitary pressures(23,24). Coronary flow reserve may be compromised even in absence of epicardial coronary artery stenosis. However concomitant atherosclerotic narrowing of coronary arteries associated with poorer prognosis (25).

Myocardial crypts:

Crypts are generally described as a normal finding in myocardium seen in population. Its prevalence is higher in phenotypically negative but genotypically positive HCM patients. The significance of amount of crypts in phenotypically positive HCM patient is not clear (26).

Autonomic dysfunction

Up to 25% HCM patients may have abnormal autonomic function which can be detected by abnormal blood pressure response to exercise. It is defined as failure to increase systolic blood pressure by at least 20 mm Hg, or a drop in systolic blood pressure during exercise of >20 mm Hg from the peak value obtained. Presence of autonomic dysfunction suggests poor prognosis (27-29).

B) Microscopic abnormalities

Many patients with similar phenotypic features can have other cause like hypertension or storage disorder and differentiation from HCM in the absence of family history and obvious genetic mutations becomes difficult. Microscopic assessment of the myocardial biopsy in such patients can help in differentiating HCM from other phenotypically similar diseases.

Myocyte disarray

Myocyte disarray is considered to be the pathological hallmark of HCM (30) which is a likely focus for fatal arrhythmia. It is characterised by regions of architectural disorganisation of hypertrophied myocytes and distinct nuclear changes. The first description of myocardial disarray was given by Teare et al (31) in patients with septal hypertrophy and history of sudden cardiac death. He had described these cases as myocardial tumour. The typical appearance of myocyte disarray has been described as a disorganized myocytes with parallel or oblique arrangement with collagen interspersed in between (12). Myocyte disarray is not specific for HCM. Many studies have also found disarray in patients with essentially normal heart, in patients with hypertension-induced heart disease, hearts of aortic stenosis patients and in patients of congenital heart disease (32). There is no consensus about the amount of myocyte disarray required to fulfil the criteria for the diagnosis of HCM. Early studies have suggested that 5–10% of ventricular septal myocardium should show disarray. In the majority of cases, myocyte disarray is extensive and >20% of the myocardium may exhibit disarray. Myocyte disarray during histology is not being used as a diagnostic criteria due to poor specificity. Varnava et al. concluded that myocyte disarray is probably a direct response to functional or structural abnormalities of the mutated sarcomeric protein (33). Recent data suggests that non-invasive detection of myocardial disarray is possible using diffusion tensor CMR imaging (34).

Myocardial fibrosis

Both macroscopic and microscopic scars are common findings in HCM. Small-vessel disease leads to blunted myocardial blood flow and myocardial ischaemia during stress in the HCM population.

The complex interactions responsible for myocardial fibrosis are only partially understood. Myocardial fibrosis presents as three mainly histopathological types-Infiltrative interstitial fibrosis, interstitial reactive fibrosis, and replacement fibrosis (Fig-1). Macroscopic scars probably represent the sequelae of an ischaemic process and correspond to histological replacement-type fibrosis. Normal hearts have a fibrillar collagen network that builds up the structural skeletal framework of the interstitium of the myocardium. The collagen network in the HCM group was morphologically abnormal and increased in size compared with structurally normal hearts which can lead to reactive type of interstitial fibrosis (35,36). A Study suggested that the HCM disease process is not only confined to disease-causing mutations in genes encoding sarcomeric proteins, but also involves connective tissue elements(37). Perhaps these abnormalities of the connective tissue elements also play a role in the pathological process leading to enlargement and elongation of the mitral valve leaflets and medial hypertrophy of intramural coronary arteries.

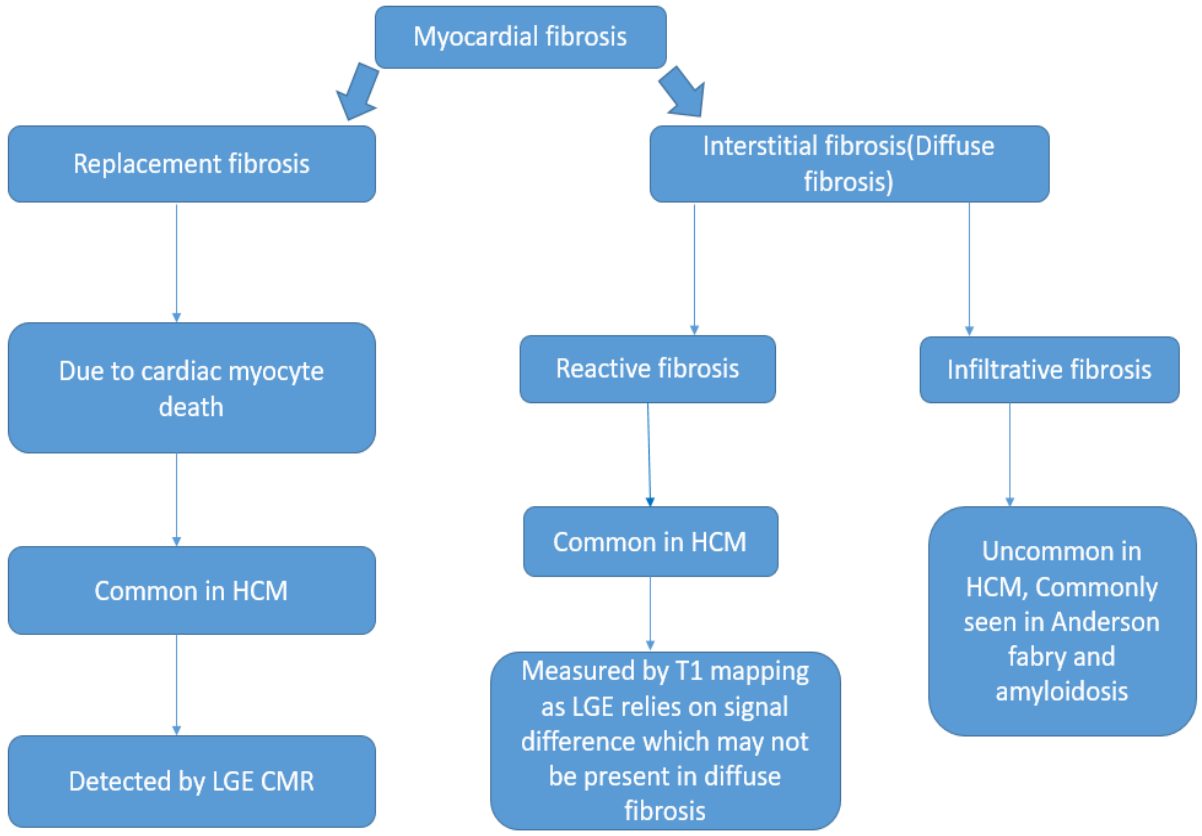


Fig 1-Types of myocardial fibrosis

Natural history and Risk stratification for SCD:

Most patients have normal life expectancy without limiting symptoms or the need for major treatments. There is increasing recognition of patients with HCM identified clinically at advanced

ages of >60 years with little to no disability. Study suggest that lifelong risk of complication due to HCM may be greater in patients with pathogenic sarcomeric gene variants or those diagnosed early in life (9). Patients may experience SCD, limiting symptoms due to LVOTO or diastolic dysfunction, heart failure and AF with thromboembolic stroke. Due to advanced cardiovascular therapies and interventions HCM mortality rates has lowered to <1.0%/year. One of the contributor in reducing mortality is categorisation of HCM patients with high vs low risk of SCD based on multiple parameters and aggressive management of high risk group.

Quantification of myocardial fibrosis

Endomyocardial biopsy is the gold standard for identification of myocardial fibrosis. Quantitative assessment of fibrosis in the limited sample can be determined by Masson trichome staining by microscopic methods (2). It gives absolute values based on the amount of collagen in the myocardial tissue. However, it is invasive and carries significant post procedural risk to the patient. EMB will be incomplete as limited samples are only possible and distribution of fibrosis will not be uniform in all locations in HCM patients. Thus it carries sampling errors and can yield false-negative results. This has been largely replaced by CMR assessment of myocardial fibrosis.

CMR Late gadolinium enhancement and quantification of fibrosis

Late gadolinium enhancement (LGE) or delayed enhancement is now considered the best investigation for assessment of myocardial viability (38,39). CMR provides accurate, non-invasive assessment of regional myocardial fibrosis using LGE, while diffuse interstitial myocardial fibrosis is accurately assessed with T1 mapping (40).LGE imaging provides an excellent depiction of macroscopic scarring initially used for myocardial infarction. LGE mainly depicts the extravascular and extracellular space in the myocardium which is increased in cardiomyopathies. Currently it is being used to detect fibrosis in non-ischemic cardiomyopathies also and in the measurement of scar resulting from treatment such as electrophysiology guided ablation (38,41,42) .Gadolinium-based MR contrast agents (GBCA) cause T1-shortening which follows the kinetics of distribution of contrast agent in the tissue. The concept is based on the delayed wash in and wash out in tissue with an increased proportion of extracellular space (e.g fibrosis). The LGE images are obtained 10–30 minutes following administration of gadolinium when there is maximum contrast between the normal and infarcted/fibrosed tissue. The contrast resolution of LGE is dependent on several factors which include the clearance rate of GBCA, the haematocrit, the ECV of the myocardium and the MR imaging parameters. Scar quantification and MR imaging for HCM is given a level 2a

recommendation in the 2020 AHA guidelines. This stresses towards the upcoming trend of inclusion of scar quantification in predicting the prognosis and also in management in the near future.

Imaging requirements

The imaging requirements of LGE include coverage of the entire heart with adequate spatial and temporal resolution. LGE imaging of LV requires a spatial resolution of 1-1.5 mm, while RV and atrial LGE requires more robust spatial resolution of 1 mm. Conventionally temporal resolution of 100-200 ms is necessary which is obtained with 10-15s breath hold protocols.

As per JCMR guideline, 2D segmented inversion recovery GRE or bSSFP, Phase-Sensitive Inversion-Recovery (PSIR), or 3D sequences should be used in patients with breath holding capacity. Single shot image with bSSFP readout (True FISP or balanced FFE) is recommended only when patient has irregular heart beat or difficulty in breath holding (44). In order to overcome cardiac motion, these IR sequences are acquired in the mid to late diastole. The IR time is chosen to best null the myocardium, as to achieve the best contrast ratio between the myocardium and the fibrotic tissue (43)

In this study we used ECG gated segmented PSIR sequence with bSSFP readout. PSIR sequence acquires both IR and proton density images at the same cardiac and respiratory phase, acquiring reference for background phase. The inversion pulse is applied every 2 RR intervals for the magnetization to completely recover. Two images are acquired for LGE assessment – a magnitude and a PSIR image. The main difference being, the PSIR sequence uses a PD readout on alternative heartbeats. PSIR sequence is not affected significantly by inversion time. Recently 3D IR LGE techniques have also been used with GRE or bSSFP readout for scar quantification. Multiple Studies compared infarct quantification with different 2D-IR and 3D-IR sequences and showed good agreement (45). Captur et al demonstrated Motion-corrected free-breathing LGE (MOCO LGE) provides high quality imaging and reduces scan time by half with good reproducibility even in very sick patient (46).

Methods for fibrosis quantification

There is no consensus regarding the technique of quantification of late gadolinium enhancement (LGE).Multiple techniques are described include manual quantification, thresholding by 2, 3, 4, 5, or 6 SDs above remote myocardium, and the full width at half maximum (FWHM) technique. All techniques rely on the fact that the LGE technique makes scar appear bright and as such can be defined as a signal intensity above normal myocardium.

I. Manual quantification: Drawing regions of interest [ROIs] around scar in all slices and sum up total volume.
II. +SD: Up to 2,3,4,5,6,SD can be used in relation to normal remote myocardium without enhancement where ROI should be drawn. ROI used to generate mean and SD for 6-, 5-, 4-, 3-, and 2-SD as thresholds for scar quantification.
III. FWHM: ROI should be placed on the enhanced myocardium which uses half the maximal signal within the scar as the threshold.

Autopsy studies have revealed myocardial scars in HCM patients with sudden cardiac death (47,48). Presence of delayed enhancement and its quantity has been correlated to wall thickness, cardiac function and ventricular arrhythmias. Estimation of the total LGE has been correlated with the risk of sudden cardiac deaths in HCM patients. Presence of LGE has been associated with an increased Odds ratio of all-cause and cardiac mortality (49). Nojiri et al concluded in their 2011 study that total LGE score can be used as a valid method to assess future cardiac events in HCM patients (47). This study used the total amount of LGE in the myocardium and correlated it with the outcome of various cardiac events.

LGE in HCM cases follows a non-ischemic pattern, predominantly in the mid myocardial or in the sub epicardial regions. Recent studies have pointed to the role of myocardial ischemia due to small coronary arteriole dysplasia as the cause of enhancement in the cases of HCM unrelated to the epicardial coronary artery distribution (76).

Spiewak et al has compared visual assessment of LGE and different thresholding techniques from 1SD to 6SD of signal intensity above normal myocardium as well as FWHM in HCM patients. They concluded that LGE quantification with the use of a threshold of 6SD above the mean SI of the remote myocardium provided the best agreement with visual assessment in patients with HCM (50).

Moravsky explored the relationship between CMR LGE and histopathological parameters including interstitial fibrosis and replacement fibrosis in patients with HCM who underwent myectomy (51). They found statistically significant correlations between CMR-LGE (at 2, 4, 5, 6, 10 SD and by the FWHM technique) analyse by pre-operative CMR, and both interstitial fibrosis and the combined interstitial and replacement fibrosis analysed from myectomy specimens. The strongest correlation was between combined interstitial and replacement fibrosis and CMR-LGE measured at 5 SD (r - 0.78, $p < 0.0001$).

Another study by Flett et al included 60 patients of different pathologies (AMI, CMI and HCM) who underwent CMR examination (52). LGE volume was quantified using the 7 techniques include manual quantification, thresholding by 2, 3, 4, 5, or 6 SDs above remote myocardium, and the full width at half maximum (FWHM) technique. They concluded that regardless of the disease under study, the FWHM technique for LGE quantification gives LGE volume mean results similar to manual quantification and is statistically the most reproducible.

SCD Risk stratification:

The presence and extent of late gadolinium enhancement (LGE) has been associated with adverse events in patients with hypertrophic cardiomyopathy (HCM),As per AHA/ACC CLINICAL PRACTICE GUIDELINE,2020, scar quantification of ≥15% of LV mass is considered high risk for SCD in HCM patients(Table-1).

Family history of sudden death from HCM	Sudden death judged definitively or likely attributable to HCM in ≥1 first-degree or close relatives who are ≤50 y of age. Close relatives would generally be second-degree relatives; however, multiple SCDs in tertiary relatives should also be considered relevant.
Massive LVH	Wall thickness ≥30 mm in any segment within the chamber by echocardiography or CMR imaging; consideration for this morphologic marker is also given to borderline values of ≥28 mm in individual patients at the discretion of the treating cardiologist. For paediatric patients with HCM, an absolute or z-score threshold for wall thickness has not been established; however, a maximal wall that corresponds to a z-score ≥20 (and >10 in conjunction with other risk factors) appears reasonable.
Unexplained syncope	≥1 Unexplained episodes involving acute transient loss of consciousness, judged by history unlikely to be of neurocardiogenic (vasovagal) etiology, nor attributable to LVOTO, and especially when occurring within 6 month of evaluation (events beyond 5 y in the past do not appear to have relevance).
HCM with LV systolic dysfunction	Systolic dysfunction with EF <50% by echocardiography or CMR imaging.

LV apical aneurysm	Apical aneurysm defined as a discrete thin-walled dyskinetic or akinetic segment of the most distal portion of the LV chamber; independent of size.
Extensive LGE on CMR imaging	Diffuse and extensive LGE, representing fibrosis, either quantified or estimated by visual inspection, comprising ≥15% of LV mass (extent of LGE conferring risk has not been established in children).
NSVT on ambulatory monitor	It would seem most appropriate to place greater weight on NSVT as a risk marker when runs are frequent (≥3), longer (≥10 beats), and faster (≥200 bpm) occurring usually over 24 to 48 h of monitoring. For paediatric patients, a VT rate that exceeds the baseline sinus rate by >20% is considered significant.

Table-1. Established Clinical Risk Factors for HCM Sudden Death Risk Stratification

In a review by Steriotis et al, Risk factors are classified into 4 categories (Table-2) which are derived from 2003 ACC/ESC and 2011 ACCF/AHA Guideline and 2014 ESC guideline except putative risk factors(53). They considered CMR LGE as a SCD risk modifier.

Major SCD risk factors

- Family history of sudden cardiac death
- Unexplained syncope
- Severe left ventricular hypertrophy
- Non-sustained ventricular tachycardia
- Abnormal blood pressure response to exercise

Additional SCD Risk factors

- Increased left atrial diameter
- Young age at the evaluation

Potential SCD Risk Modifiers

- Left ventricular outflow tract obstruction
- Late Gadolinium enhancement on CMR Imaging
- Genetic Mutations
- Left ventricular apical aneurysm
- End-stage phase of HCM (EF <50 %)

Putative SCD risk factors

- Paced ventricular electrogram fractionation
- QRS fragmentation on the ECG
- Exercise-induced NSVT/VF
- Severe obstructive coronary disease
- Microvascular ischaemia
- Midventricular obstruction
- Atrial fibrillation

Table-2.Major SCD risk factors(ACC,ESC,ACCF,AHA guidelines),modifiers(ACCF/AHA guidelines) and additional SCD risk factors (ESC guidelines) used in the current guidelines and putative risk factors described in the literature but not included in the current guidelines.

In a meta-analysis by Green et al which included 4 studies and 1063 patients, predictive value of LGE on CMR was analysed for future cardiovascular events and death. They concluded that LGE by CMR has prognostic value in predicting adverse cardiovascular events among HCM patients. There are significant relationships between LGE and cardiovascular mortality, heart failure death, and all-cause mortality in HCM. Additionally, LGE and SCD/aborted SCD displayed a trend toward significance. The assessment of LGE by CMR has the potential to provide important information to improve risk stratification in HCM in clinical practice (55).

Chan and colleagues suggested that extent of LGE was associated with an increased risk of SCD events and in particular LGE ≥15 % of the LV mass demonstrated a twofold increase in SCD event rate in those patients who would otherwise considered be at low risk. Recent studies suggest that the extent of LGE (>15% of the myocardial mass) can play a major role in SCD stratification in this subset of patients (56).

A study by Christina Doesch has established incremental benefit of LGE CMR for risk stratification in addition to ESC risk stratification. They compare CMR characteristics of 149 patients classified according to ESC risk stratification criteria into low, intermediate and high risk for SCD. Patients with a high ESC risk score revealed a significantly higher extent of LGE compared to patients with intermediate or a low risk scores. During follow-up of 4 years an extent of LGE ≥20% identified patients at a higher risk for major adverse cardiac arrhythmic events in the low and intermediate ESC risk group whereas an extent of LGE <20% was associated with a low risk of major adverse cardiac arrhythmic events despite a high ESC risk score ≥6% (57).

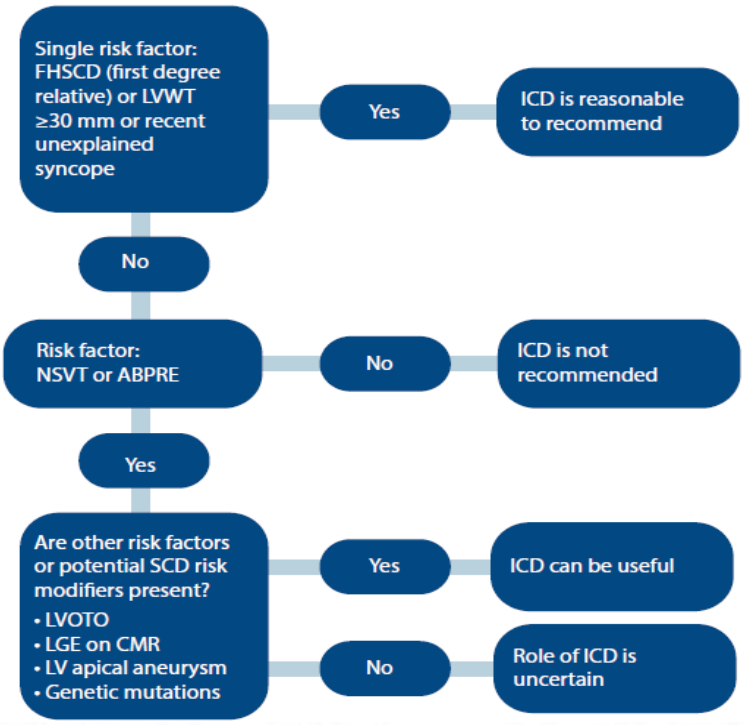


Fig-2.2011 ACCF/AHA model for ICD implantation for primary prevention in HCM.

A recently published study by Marone et al suggest enhanced ACC/AHA guideline based risk factor strategy prospectively predict SCD events in nearly all high risk patients with HCM, resulting into prophylactically placed ICDs that prevented many catastrophic events. They included LGE CMR, End stage disease defined by LVEF <50% and LV apical aneurysm in addition to ACC/AHA risk stratification criteria. This enhanced ACC/AHA clinical risk factor strategy was highly sensitive for predicting SCD events (range, 87%-95%) but less specific for identifying patients without SCD events (78%).It shows good discrimination between patients who did or did not experience an SCD event. In comparison, European Society of Cardiology risk score was much less sensitive than enhanced ACC/AHA criteria, consistent with recognizing fewer high-risk patients (58).

On the similar line, Freitas et al conducted multicentric retrospective analysis of HCM patients who underwent CMR for diagnostic confirmation and/or risk stratification. Eligibility for ICD was assessed according to the HCM Risk-SCD score and the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) algorithm. The amount of LGE showed greater discriminative power than the ACCF/AHA and the HCM Risk-SCD. They concluded that the amount of LGE seems to outperform the HCM Risk-SCD score and the ACCF/AHA algorithm in the identification of HCM patients at increased risk of SCD and reclassifies a relevant proportion of patients (59).

A recent meta-analysis that included over three thousand individuals with HCM, highlighted the relationship between LGE and cardiovascular mortality in HCM. This study further proves that extensive LGE is a promising risk-stratification tool as it significantly predicts SCD risk, cardiac mortality, and all-cause mortality in patients without conventional risk markers. Hence, LGE should be considered a novel risk marker in predicting SCD in HCM (60).

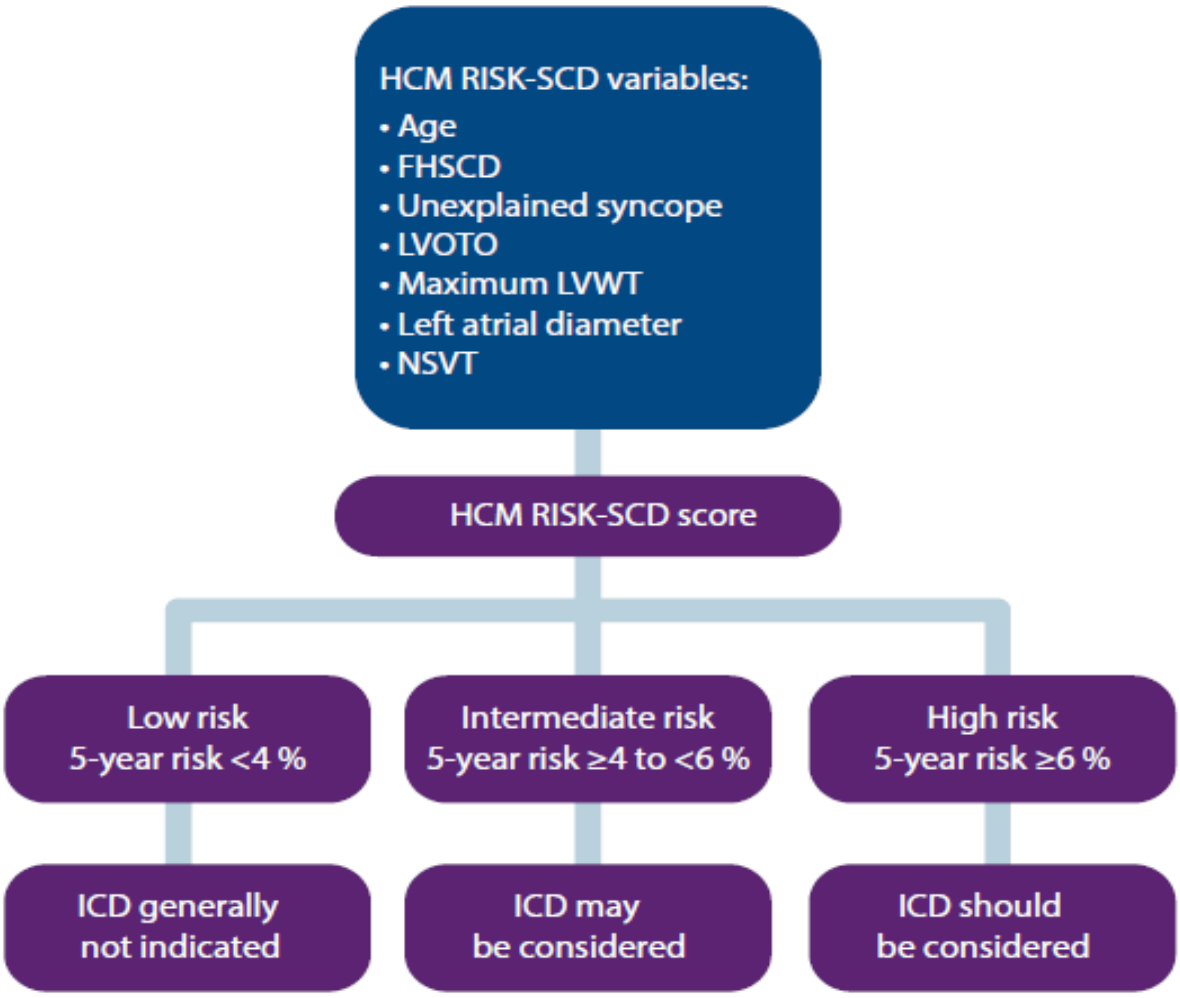


Fig-3. 2014 ESC model for ICD implantation for primary prevention

Despite these evidences, ESC 2014 guideline (54) does not recommend CMR LGE quantification to stratify patients into high, intermediate and low risk category for SCD before considering ICD implantation in HCM patients (Fig-3).

Selvester scoring/QRS score

In 1972, Selvester QRS score was described to obtain information regarding scar size and location from the cardiac electrical activity from the computer simulations. Though it has been externally validated in comparison to autopsy-measured myocardial infarct and shown prognostic value, it did not achieve widespread clinical use because of confounding factors. However due to widespread use of ICDs and CRT for which patient selection is key for optimal outcome, there is renewed interest in QRS scoring. Older version of QRS scoring could only be used in the absence of ECG confounders (i.e. bundle branch/fascicular blocks and ventricular hypertrophy), which makes QRS scoring impractical for ICD/CRT patient selection because greater than 50% of potential ICD/CRT patients have ECG confounders. In 2009, modified Selvester score was proposed which described how to apply the QRS score in the setting of hypertrophy and conduction defects (Confounders). This was made possible by using adjusted criteria for each of the confounding abnormalities: left and right ventricular hypertrophy (LVH, RVH), left anterior fascicular block (LAFB), left bundle branch block (LBBB), right bundle branch block (RBBB), RBBB + LAFB, and no confounders. However, these changes also introduced additional complexity and nuance to the scoring procedure. The scoring criteria sets differ slightly among all of these abnormalities with LBBB having the most dissimilar criteria, but they still follow the same principle of a score with each point representing 3% infarct of the LV myocardium and the maximum number of points was 32 (61).

Application of QRS Scoring/Modified Selvester scoring

Younger males have higher voltage and older females have lower voltages which can give false positive points during calculation. Before scoring, all absolute amplitude criteria (not ratios) are corrected to the age of 55 in the scoresheet by increasing them 1%/year for those aged 54 years and below and decreasing them 1%/year for those aged 56 years and above. For females, both duration and absolute amplitude (not ratio) criteria are further decreased by 10% (62).After ECGs have been categorised according to confounders and amplitude and duration are corrected, the QRS score for that confounder type is selected and applied.

Strauss et al has compared QRS scoring with CMR in 62 patients of ischemic or non-ischemic dilated cardiomyopathy with LVEF<35% prior to placement of ICD for primary prevention of SCD. They showed correlation of r=0.74, (P<0.0001) between CMR and Selvester scoring. They concluded that QRS scores identify and quantify scar in ischemic and non-ischemic cardiomyopathy patients despite ECG confounders (63). Higher QRS-estimated scar size is associated with increased arrhythmogenesis and warrants further study as a risk-stratifying tool.

Studies have shown that QRS score can enhance prediction of which patients will experience appropriate ICD shocks and respond to CRT (64).

Same author has performed another correlation analysis in a cohort of symptomatic Chagas disease where they found correlation coefficient of r=0.69 between CMR LGE scar and QRS score. They concluded that, QRS score can be used as a screening tool and may enhance risk stratification in patients with Chagas disease (65).

Bignoto et al has published utility of QRS scoring in HCM cohort and compared with the scar quantification by delayed enhancement on cardiac CT. They found correlation of r=0.70, $p<0.01$. They concluded that The Selvester QRS score provides reliable quantification of myocardial fibrosis and was well correlated with MDCT in patients with HCM (66).

Another cross sectional analysis by Qian suggest baseline Selvester QRS scores and changes in QRS scores independently predicted poor outcomes in patients with acute STEMI who underwent PCI (67).

In the study by James Rosengarten and colleagues it was found that QRS scoring best corresponded when the scar was transmural. They also showed that association of QRS score was with medium term mortality risk, but not with risk of ventricular arrhythmia. It may be that the score is best suited as a risk stratifier of those with least potential to benefit from ICD. They showed moderate correlation between CMR scar and QRS score for transmural enhancements (r=0.49, $p<0.001$) (68).

In the APEX AMI trial, modified Selvester score was calculated in 143 patients with STEMI who underwent primary PCI and survived to hospital discharge. After multivariable adjustment, patients with higher QRS scores remained more likely to develop an adverse outcome versus those with QRS scores ≤ 3 (69).

LACUNAE IN LITERATURE

There is already sufficient data available about utility of modified Selvester score in ischemic cardiomyopathy for scar quantification as well as patient selection for ICD/CRT and prognostication. However evidence on clinical use of Modified Selvester score in non-ischemic cardiomyopathy is sparse. Ischemic cardiomyopathy has usually homogenous and dense scar along the particular coronary artery territory but in case of non-ischemic cardiomyopathy scar is usually more diffuse and heterogeneous. So this study aims to assess utility of QRS score in cohort of HCM patients with non-transmural and heterogeneous scar. In future, score may be helpful to stratify HCM patients which is the primary objective of assessing scar.

MATERIALS AND METHODS

Study design

This was an analytical cross sectional study conducted in the Department of Imaging Sciences and interventional radiology in association with the Department of Cardiology from July 2019 to June 2021 after obtaining the institutional ethics committee approval. Informed consent was obtained from all the participants in English and local language (Malayalam).

Inclusion criteria:

All consecutive patients suspected of having HCM based on echocardiography (Max wall thickness ≥15 mm) with age >18 years, referred for cardiac MRI evaluation from July 2019 to June 2021 had been included irrespective of any gender or ethnicity bias.

Exclusion criteria:

- Patient or relatives declining consent.
- Patients age under 18 years, Pregnancy.
- Patients who have alternative diagnosis by MDT at the end of cardiac MRI study.
- Patient with a known diagnosis of metabolic/infiltrative diseases, ischemic cardiomyopathy, previous ICD implantation, myectomy or alcohol septal ablation.
- Claustrophobic patients, patients with MR incompatible metallic implants, pacemakers or cochlear implants and other contraindications to cardiac MR.
- Contraindication for MR contrast.

Study design flow:

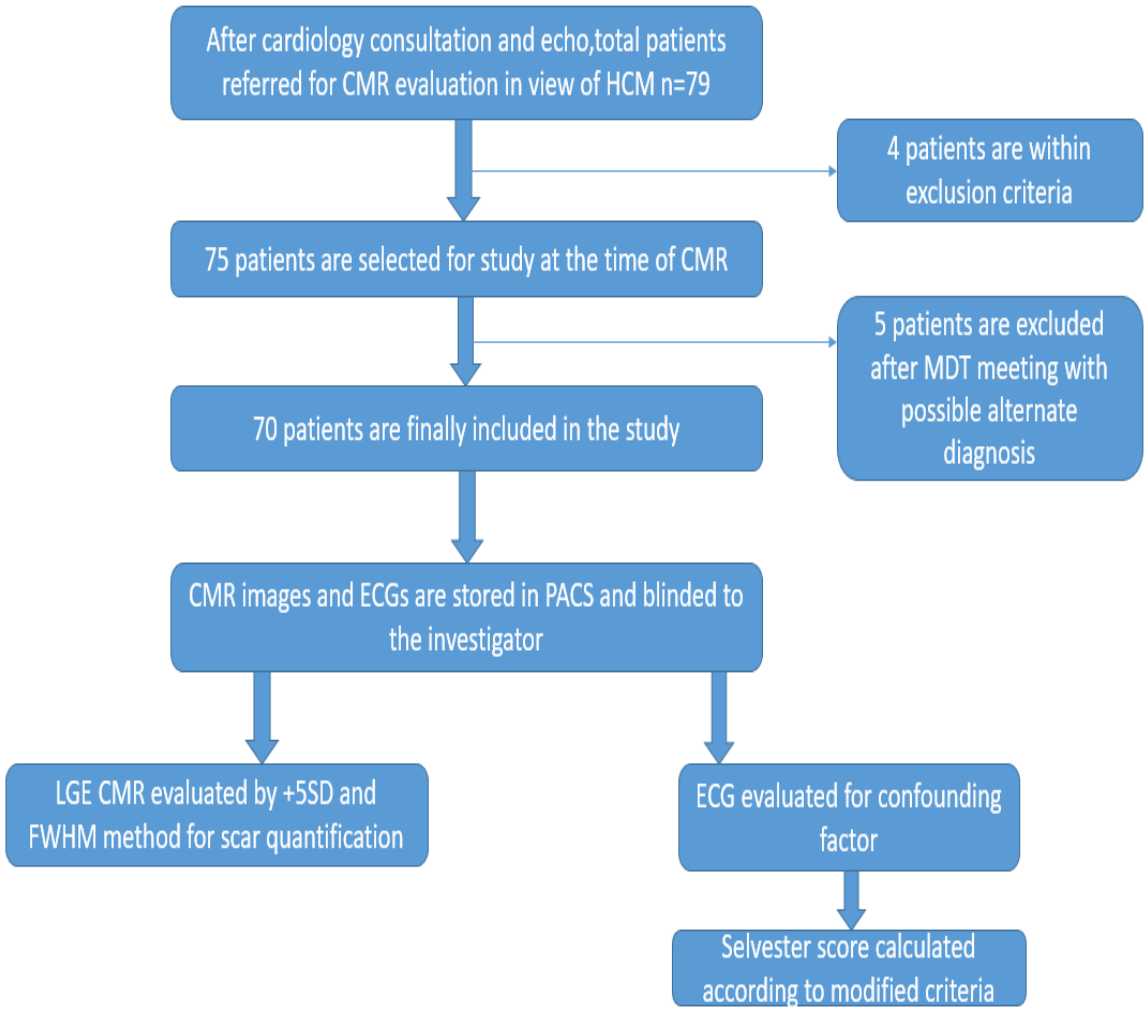


Fig-4.Study design and flow chart

We selected 70 consecutive patients who had undergone CMR imaging for HCM, with the imaging characteristics matching the inclusion criteria and the exclusion criteria. Few subjects are excluded from analysis after MDT meeting where conclusive diagnosis of HCM was not made or CMR image quality was sub optimal. For the study, CMR images were obtained from picture archiving and communication system (PACS), anonymized and stored separately in numbered folders. These images were post processed and analysed by a reader with 4 years of experience in interpreting CMR studies. The primary diagnosis, the symptomatology, associated comorbidities, and relevant investigation were recorded for the enrolled patients which included electrocardiogram, echocardiogram, and chest x-ray as a part of the routine investigation. All transthoracic echocardiography was performed by experienced sonographers (4 years' experience) using commercially available ultrasound equipment (Phillips iE 33) according to American Society of

Echocardiography guidelines. The echocardiographic findings were carefully recorded for further correlation and planning the CMR study.

CMR Protocol:

CMR examinations were done on 1.5 T Siemens (MAGNETOM Avanto/Siemens Healthcare, Erlangen, Germany) equipped with a 36-element dedicated cardiac array. The standard clinical HCM CMR protocol consisted of scout images followed by functional assessment of the left ventricle using cine steady-state free precession techniques and post contrast LGE images using PSIR b-SSFP sequence.

Total acquisition time was 40 min.

Imaging parameters are described in table-3.

	Siemens 1.5 T Magnetom Avanto		
Parameter	Scout	Cine images	10 min LGE PSIR
TE	1.11	1.15 ms	3.2
TR	247	43 ms	769
Flip angle	80	57	25
FOV	400 mm	340 mm	340 mm
Matrix size	256x128	192x192	256x256
Slice thickness	10 mm	8 mm	8 mm
Time of inversion	-	-	Adjusted to null myocardium
ECG gating	None	Retrospective	Prospective
Breath hold	No	Yes	Yes
Spatial resolution	3x3x10 mm	1.8x1.8x8mm	1.5x1.5x8 mm

Interslice gap	-	2mm	2 mm
SNR	1	0.9-1	0.9-1

Table-3.CMR protocol and parameters

Cine images

Cine images were obtained using Retrospective electrocardiographic gating in short axis,4 Ch ,2 Ch and 3-ch view(Fig-5). Total 20 cardiac phases acquired during one R–R interval with temporal resolution <60 ms between phases. Bright blood imaging technique using Balanced SSFP (Tru FISP/FIESTA) sequence was applied to obtain CINE images in various orthogonal views. Short axis stack covers from base to apex. Allows for assessment of global and regional ventricular function, calculation of LV and RV volumes, ejection fraction and LV mass. 2 chamber view gives a view of the anterior and inferior wall of the left ventricle with the mitral valve view. Applications include evaluation of the anterior and inferior wall motion with the assessment of the left atrial appendage and mitral valve. 4 chamber view was acquired by placing a slice bisecting the highest curvature of the right ventricle. It was useful for assessment of the septal and lateral wall motion of the left ventricle, involvement of apex, mitral & tricuspid valve function, size, and function of the right ventricle.

LGE sequence:

LGE images were obtained 10 minutes after administrating Gadolinium-based contrast medium (Gadotrast, Gedoterate Meglumine ,Unique pharmacceuticals, India) intravenously at 0.1 mmol/kg body weight. Breath-hold segmented ECG gated PSIR b-SSFP sequence performed in the same orientation as the cine images. The inversion time was adjusted to completely null normal myocardium (Typically 250-400 ms)(Fig-7).

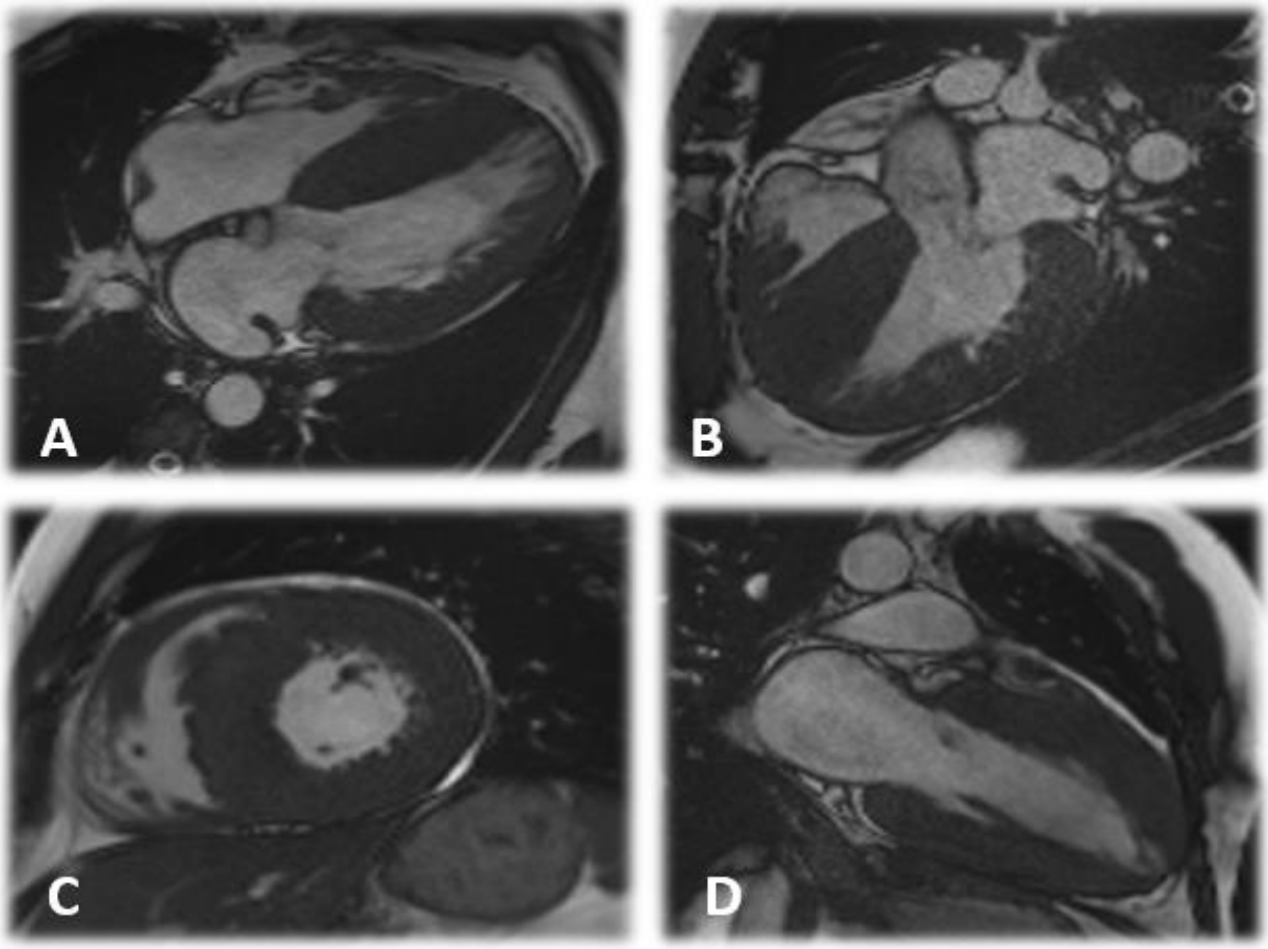


Fig-5. A, Cine 4 chamber; B, Cine LVOT; C, Cine short axis; D, Cine 2 chamber view obtained using bSSFP with retrospective gating. Short axis and the 4-chamber view reveal the asymmetric thickening of the interventricular septum.

Image analysis:

CMR data were analysed using commercially available post-processing software. LV volumes, ejection fraction, myocardial mass, and extent of myocardial LGE were measured by offline analysis using Cvi42 (Circle Cardiovascular Imaging, Calgary, Alberta, Canada) by a single experienced reader (4 years of CMR experience).Cine images were used to measure LV ejection fraction and volumes by tracing the endocardial and epicardial boundaries at the end-diastole and end-systole. Ejection fraction and myocardial mass were obtained using the semi-automated technique. Papillary muscle were excluded from the myocardial mass. Maximum wall thickness was calculated by software as an area of myocardium with max thickness after epi and endocardial contouring (Fig-6 & 7).

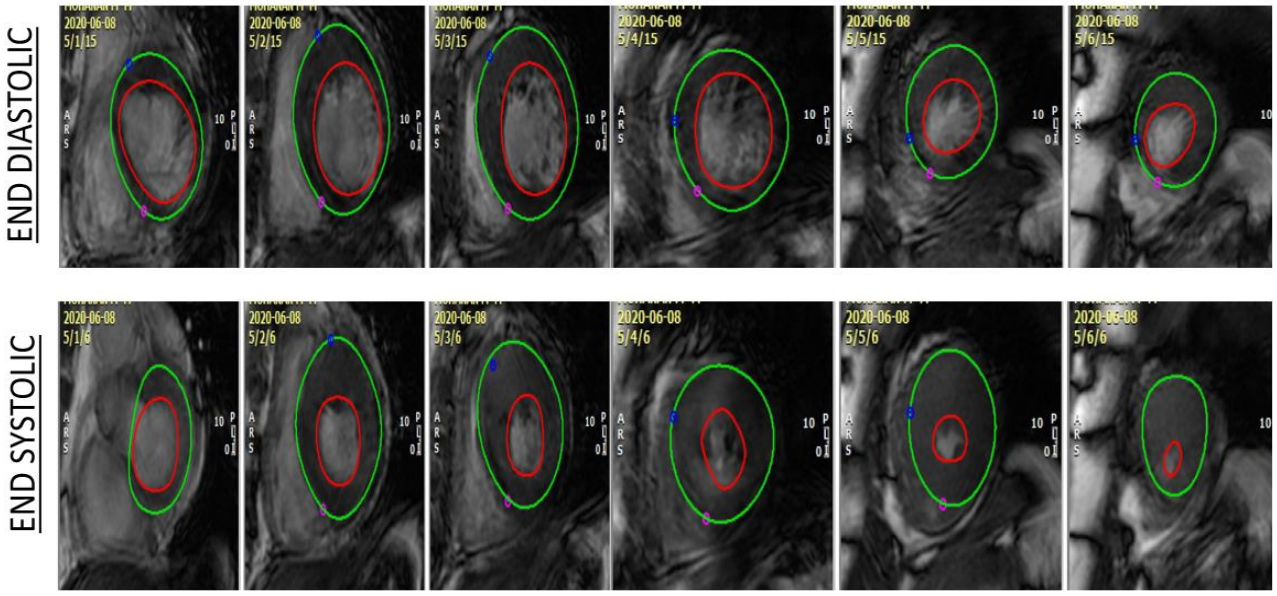


Fig-6.Calculation of LV function by end diastolic and end systolic phase contouring

LGE images were used to measure total scar size for the entire LV. LGE was expressed as percent of total LV mass. LGE was calculated using 2 methods (+5SD and FWHM).Two user-defined free hand regions of interest were chosen.

1) Within normal nulled (with no enhancement) remote myocardium to generate the mean and +5SD(Blue contour in fig-7).
2) another region of interest was drawn in hyper intense myocardium(Detected by +5SD method) and used to define the maximal signal for the FWHM threshold.(Pink contour in fig-7)

Any areas that were identified as enhancement by the software, but cross verified by the reader to represent inversion time artefact or contamination by blood pool/pericardial fat were excluded manually by contour adjustment or exclusion tool available in software. Total LGE was determined on a per-patient basis for each semi-automated technique as the sum of LGE area for each slice multiplied by the slice thickness.

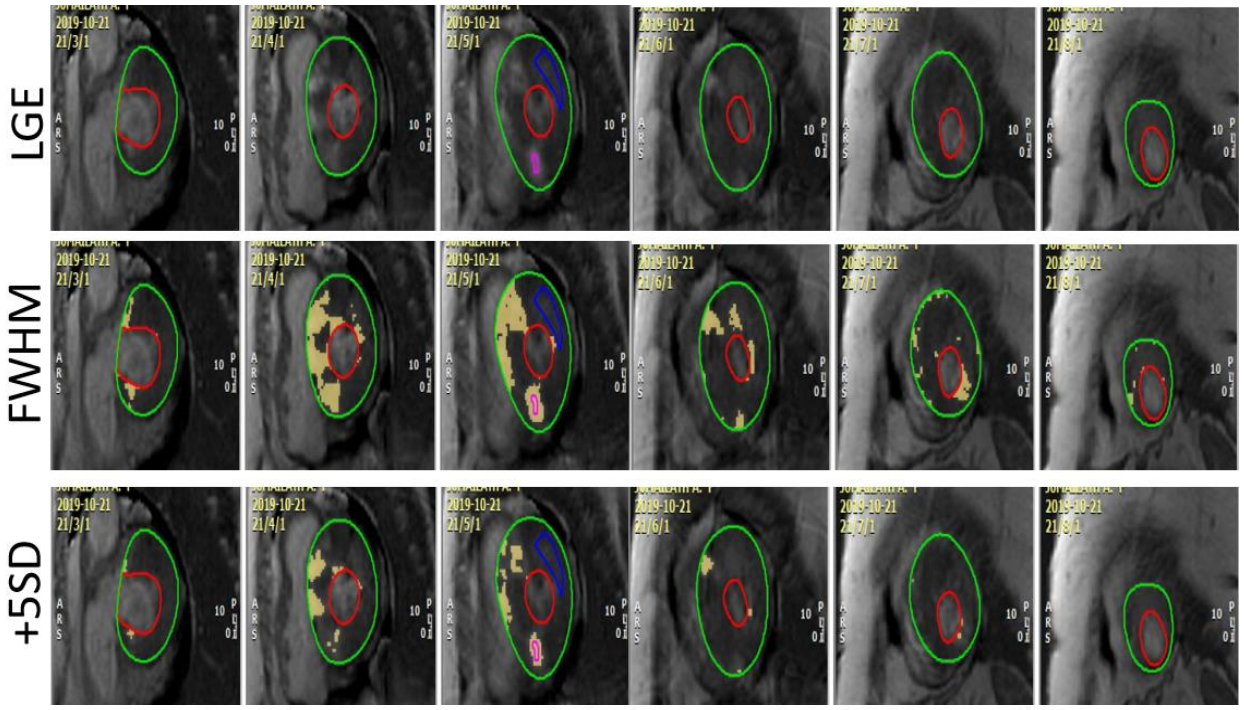
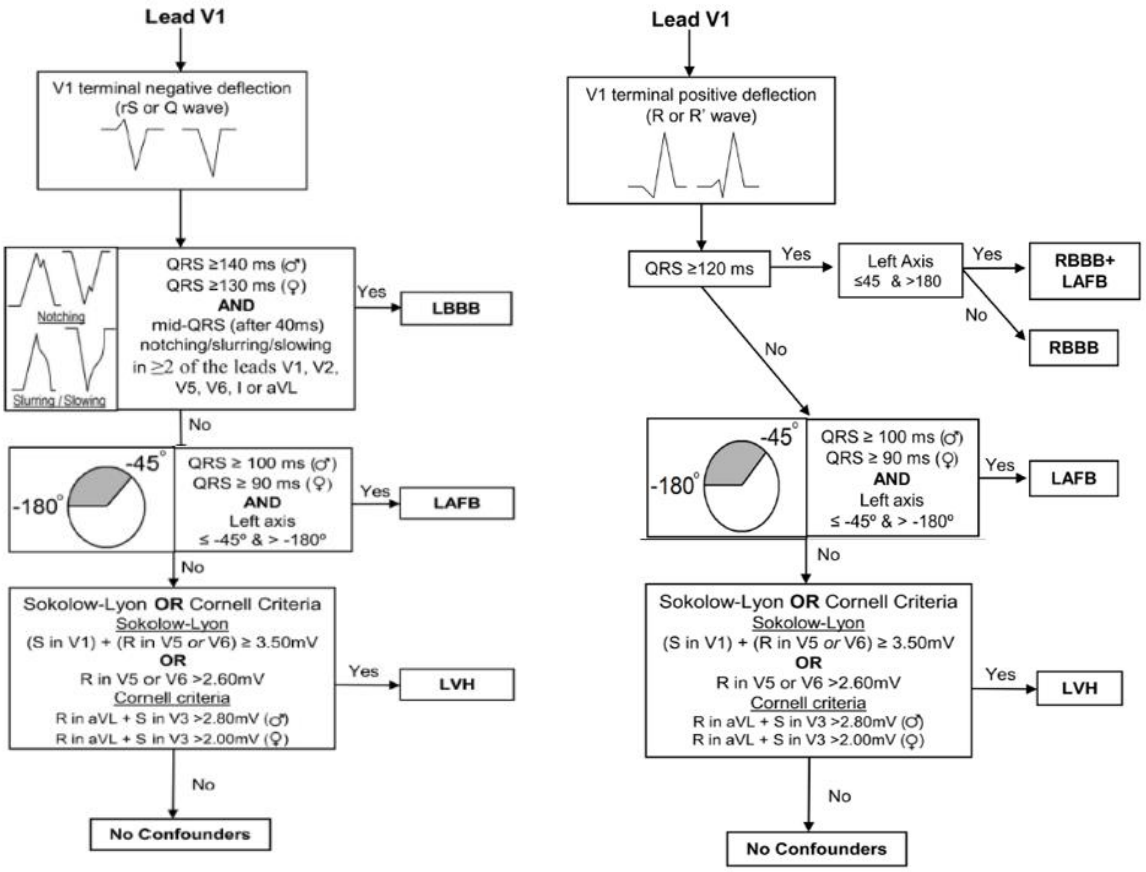


Fig-7.Scar quantification by +5SD and FWHM methods

ECG Acquisition and Analysis

12-lead ECG was acquired as a routine work up before patient undergo CMR examination. ECGs were first analysed for the presence of confounders (left bundle branch block, left anterior fascicular block, right bundle branch block, RBBB plus LAFB, and left ventricular hypertrophy) according to the pre specified definitions mentioned below (Fig-8)

QRS-score criteria were then applied for the specific underlying conduction type present (Annexure 1). The amplitudes of the Q, R, and S waves and the durations, amplitude ratios, and notches then were measured. There are 32 possible total points, and each point represents 3% of the LV mass. QRS scores for RBBB, LAFB, LAFB-RBBB, and LVH have relatively minor differences from the no confounder QRS score; however, the LBBB score is fundamentally different because the electrical activation wave front has to proceed through the ventricular septum before activating the myocardium. Selvester score calculation were verified by a cardiologist with expertise in electrophysiology (> 6 years experience). ECG used for Sylvester scoring were taken on the same day as Cardiac MRI.



Example:

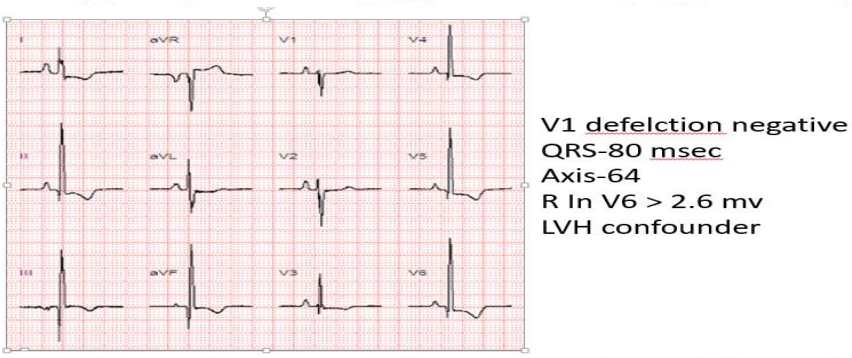


Fig-8 Assessment for confounding factor

OBSERVATIONS AND RESULTS

Statistical analysis

The collected data were analysed with IBM SPSS Statistics for Windows, Version 23.0(Armonk, NY: IBM Corp) and the graphical representation of the data was made using the Microsoft excel 2016 software. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To assess the relationship between the variables Pearson's Correlation was used. To demonstrate agreement between 3 methods, bland Altman plots were used. The Receiver Operating Characteristic curve analysis was used to find the efficacy of the variables with Sensitivity ,Specificity, PPV, NPV and accuracy.In both the above statistical tools the p-value 0.05 is considered as significant level.

As part of the study, finally a total of 70 cardiac MRI study subjects were processed for quantitative scar evaluation along with 12 lead ECG.

DEMOGRAPHICS

1. Gender distribution:

Of the 70 patients,75.7%(n=53) were male and 24.3% (n=17) were female. Male to female ratio of the subjects was 3:1 in this study. Although male predominance may reflect a similar lack of awareness that is well recorded in other cardiovascular diseases in women, the difference in disease expression among the sexes is likely to be influenced by genetic and endocrine factors. Women are more prone to heart failure–related mortality and HCM-related complications. Though data is insufficient, oestrogens have been shown to exert preventive effects on cardiac hypertrophy (70).

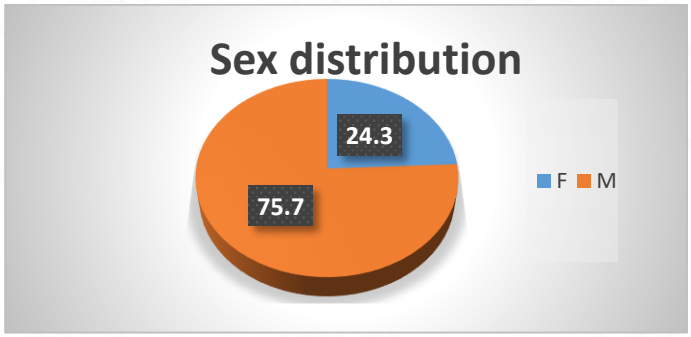


Fig-9. Frequency distribution of sex in the study population

2. Age distribution:

The minimum age was 19 years and the oldest patient was 71 years with a mean age of 49.7 years in the study population. The majority (51.2%, n=36) of the study subjects were in the age group of 40-60 years. It is similar to described in the literature where first diagnosis of HCM usually made during 4th or 5th decades (2). Mean age of our cohort was 49.7 years. In recent years, older patients with HCM have been increasingly recognized because of greater awareness of the disease and advances in cardiac imaging techniques. While younger patients rarely develop heart failure-related issues, an early onset of disease is associated with markedly increased risk of HCM complications after midlife (70). Patient age importantly dictates the clinical course for many patients with HCM. Aging may represent a negative risk marker for sudden death to many HCM patients. HCM patients of advanced age are more likely to die of non-cardiac competing morbidities than

of HCM. Recommendations for primary prevention ICDs in older HCM patients should be made on a case-by-case basis with prudent restraint (71).

Table-4:Age distribution in the study population		
Age group	frequency	Percent
18-40 years	16	22.85
40-60 years	36	51.42
>60 years	18	25.71
Total	70	100

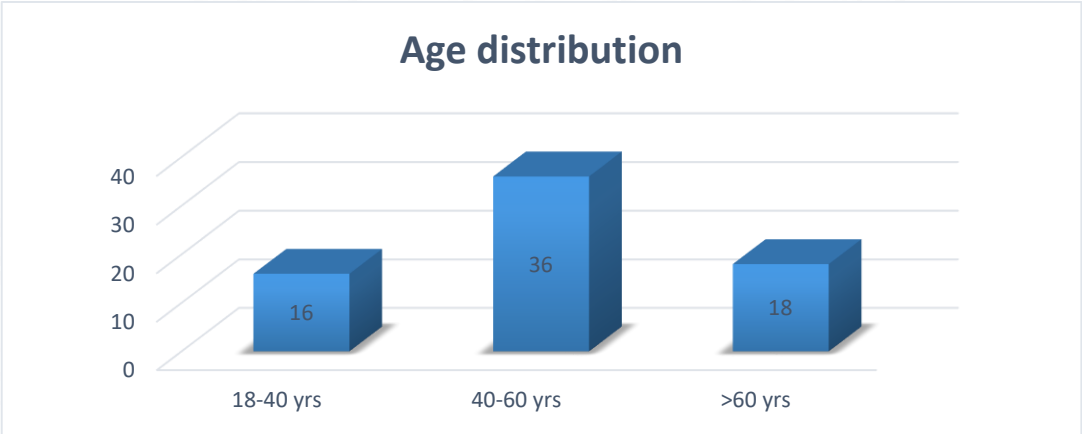


Fig-10 : Age distribution in the study population

3. Comorbidities:

Comorbidities of the study population that were analysed included HTN, DM and dyslipidaemia. Hypertension (41.4%) was the most commonly associated comorbidity in the study population followed by dyslipidaemia(28.6%)and Diabetes(14.3%). Although HTN can cause LVH, it is usually symmetrical & global and rarely >15 mm in thickness. Presence of RVH, Family history or repolarisation abnormality also suggests HCM(9). Hypertension (41.4%,n=29) was the most common comorbidity present in the study population followed by dyslipidaemia and diabetes. In a recent study, hypertension was an independent predictor of outcome in patients with HCM, irrespective of ethnicity, sex, or age(70). Aggressive management of hypertension is therefore mandatory in HCM, but may be challenging, as most vasodilators will exacerbate dynamic LVOT obstruction.

Table-5 :Comorbidities in study population		
	Present	Absence
Hypertension	29(41.4%)	41(58.6%)
Diabetes mellitus	10(14.3%)	60(85.7%)
Dyslipidemia	20(28.6%)	50(71.4%)

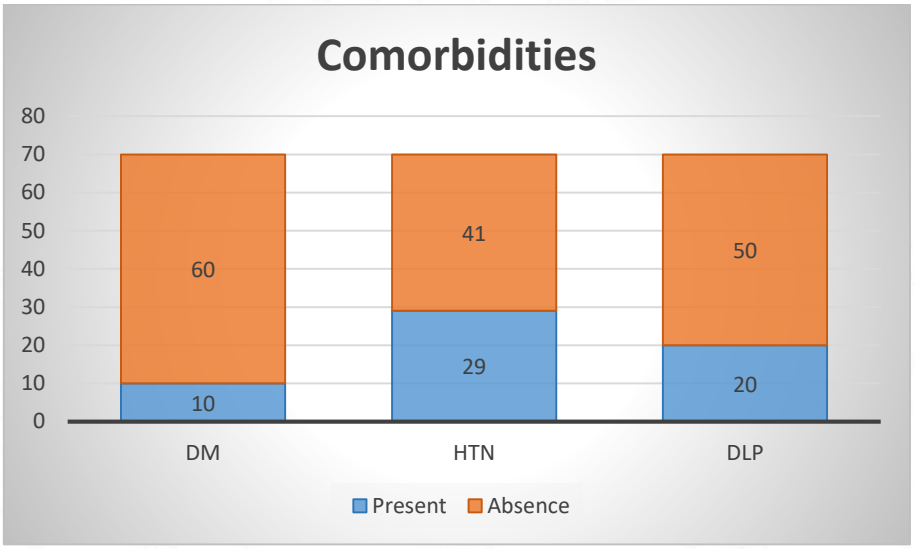


Fig-11:Comorbidities in Study population

CLINICAL PRESENTATION:

Most common presenting symptom in our patients was dyspnoea on exertion (94.3%, n=66). History of single or multiple episodes of syncope was present in 54.28 % (n=38).Palpitation was present in 52.9 %(n=37).However, most of the patients presented with multiple symptoms, the most common being NYHA class II Dyspnoea with syncope and/or palpitation.

Table-6:Clinical presentation		
	Present	Absent
Dyspnoea	94.3%(n=66, NYHA class II/III)	5.7%(n=4,NYHA class I)
Syncope	54.28%(n=38)	45.72%(n=32)
Palpitation	52.9%(n=37)	47.1%(n=33)

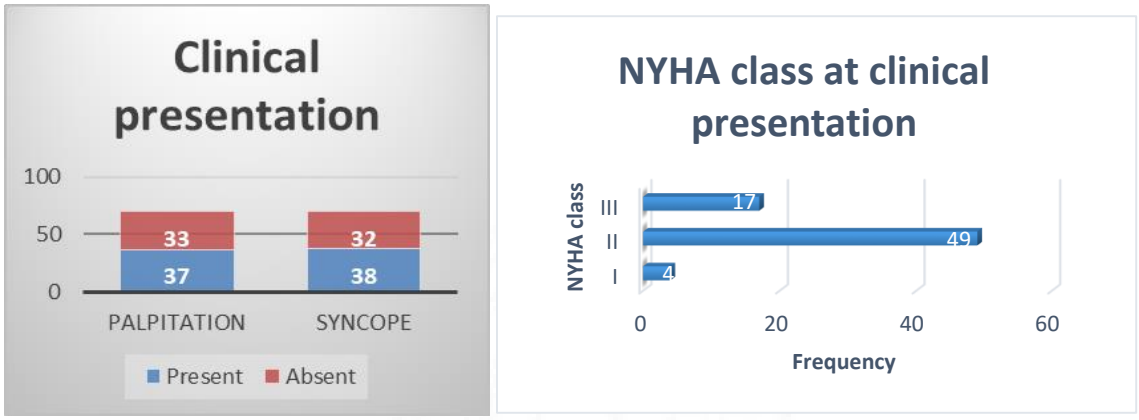


Fig-12.Frequnecy of Clinical presentation

FAMILY HISTORY OF HCM OR HCM RELATED SCD:

24.3%(n=17) of the study population had a family history of HCM or HCM related SCD. However genetic studies were not available at the time of study in these patients.

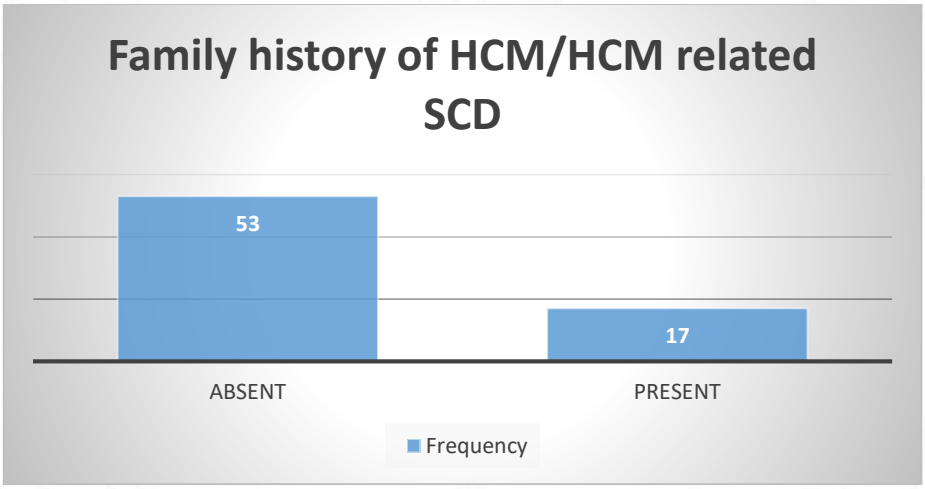


Fig-13 Frequency of Positive family history

HOLTER STUDY:

20 %(n=14) patient has abnormal 24 hr Holter study which includes Non-sustained ventricular tachycardia defined as an ectopic ventricular rhythm with wide QRS complex (≥120 milliseconds), rate faster than 100 bpm, lasting for at least 3 beats and spontaneously resolves in less than 30 seconds. NSVT which are frequent(≥3 occurrence),longer(≥10 beats) and faster (≥200 bpm) is considered high risk factor for sudden cardiac death with a hazard ratio of 2.89(9). As a routine protocol all the patient underwent 24 hrs ambulatory Holter monitoring. Sub analysis suggest patients with NSVT shows higher Scar (by all

scar quantification methods) in comparison to patients who are having normal Holter study which is statistically significant (P<0.005)

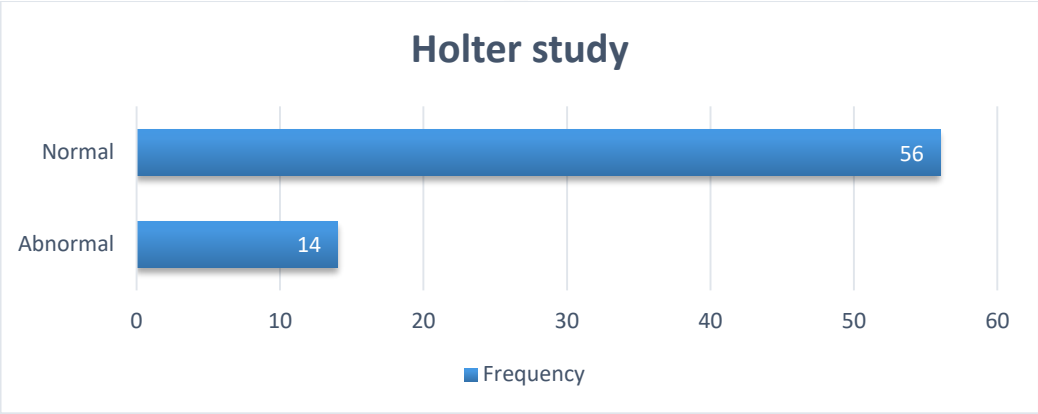


Fig-14.Frequnecy of abnormal Holter study

	Normal Holter study(N=56)	Abnormal Holter(NSVT)(N=14)	P Value
Selvester score mean	6	18.42	<0.005
5SD mean	6.38	17.43	<0.005
FWHM mean	14.63	23.59	<0.005

Table -7.Mean Scar difference between patients with abnormal and normal Holter study

CONFOUNDERS:

Most common confounder present in this cohort was hypertrophy of left ventricle followed by left anterior fascicular block (LAFB). RBBB, RBBB+LAFB or LBBB were infrequent.

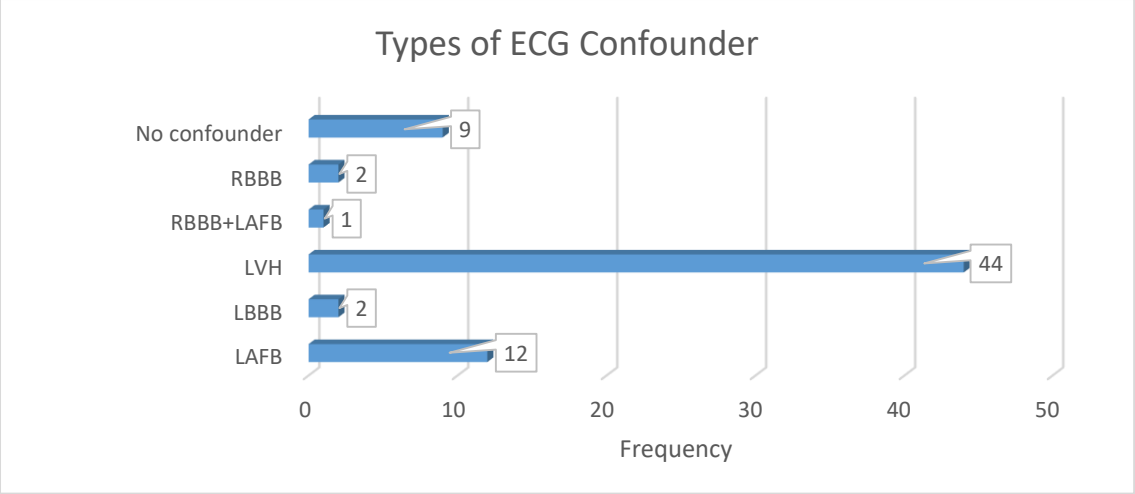


Fig-15.Frequency of confounders

DESCRIPTIVE ANALYSIS

	Variable	Mean ± SD	Range	
1	Age	49.7 years(±12.6)	19-71 years	
2	CMR LVEF	69.8%(±8.3)	42%-82.4%	
3	LGE by 5SD	9.3%(±9.9)	0.1%-46.1%	No significant difference among the mean by 3 methods
4	LGE by FWHM	10.3%(±10.7)	0%-44.7%	
5	Scar by Selvester score	9.2%(±7.6)	0%-36%	
6	Absolute LV Mass	159.2gm(±50.5)	92.1-321.9 gm	
7	Index LV Mass	92.5 gm/m2(±24.9)	57-150.1 gm/m2	
8	Max LV wall thick ness	20.1mm(±4.3)	15-32.5 mm	

Table-8.Mean and SD of various measurements

Average maximum wall thickness measures 20.1mm (±4.3 mm) with only 4 patients satisfied the criteria for massive hypertrophy (>30 mm).Massive hypertrophy is considered as a risk factor for SCD.

DISTRIBUTION

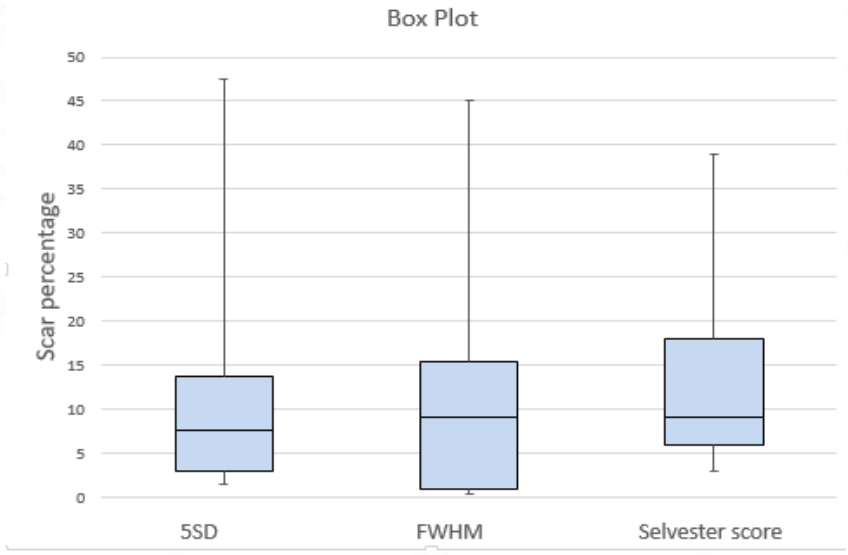


Fig-16.Box and Whisker plot for median and range comparison

Comparative analysis by Box and Whisker plots suggest boxes and median by all 3 methods overlap with each other suggestive of no significant difference between methods.

CORRELATION ANALYSIS

1.Correlation between scar measurement by CMR LGE technique with 5SD method and FWHM method: Strong Positive correlation exists between 2 methods of scar measurement by CMR LGE (r=0.848,p-0.0005)

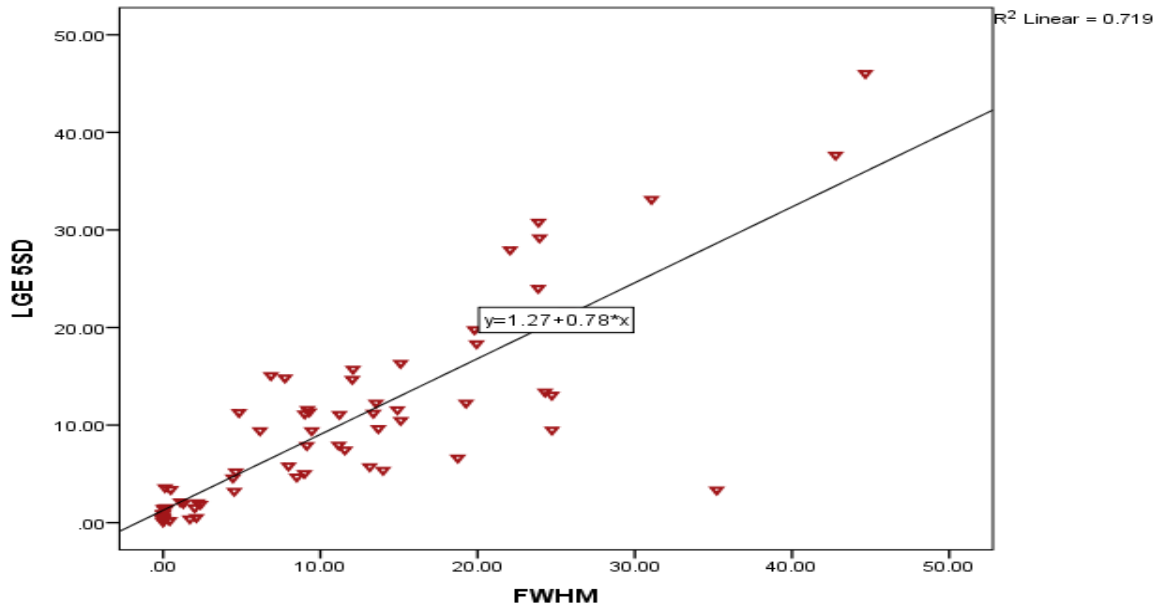


Fig-17. Correlation between 5SD and FWHM

2. Correlation between scar measurement by Selvester scoring system and CMR 5SD method: Strong positive linear correlation demonstrated between these 2 methods(r=0.813,p-0.0005).By this correlation CMR LGE can be estimated using correlation equation y=0.43+1.06x where y=Scar percentage by CMR LGE and x=Scar percentage by Selvester score.

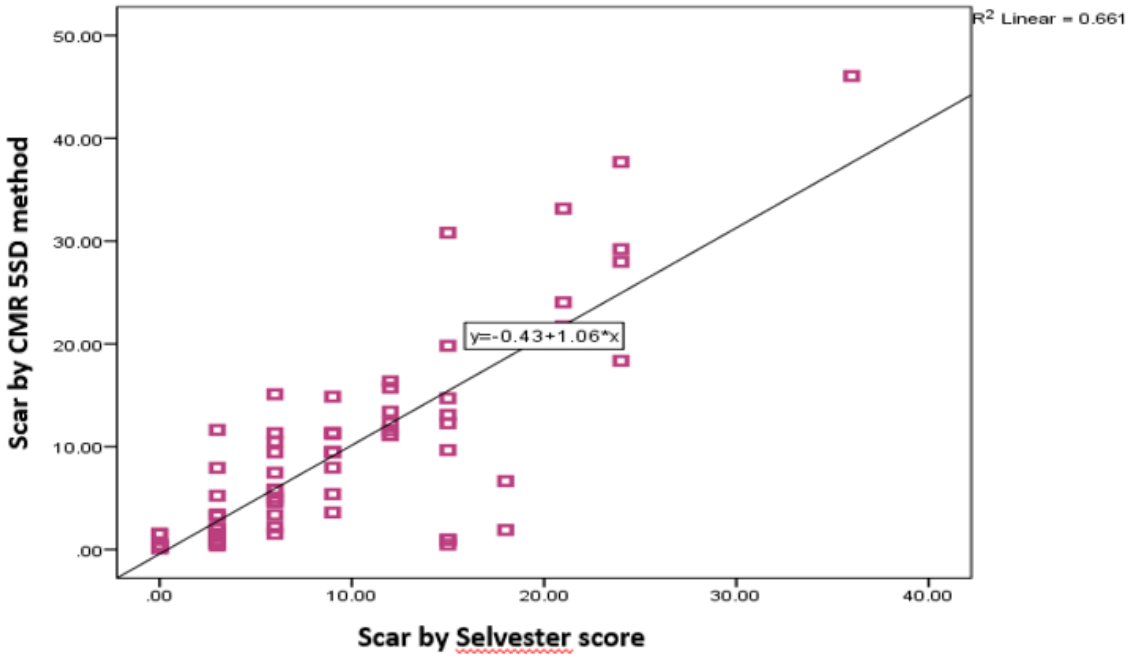


Fig-18. Correlation between 5SD and Selvester score

3. Correlation between scar measurement by Selvester scoring system and CMR FWHM method: Strong positive linear correlation demonstrated between these 2 methods(r=0.751, p-0.0005)

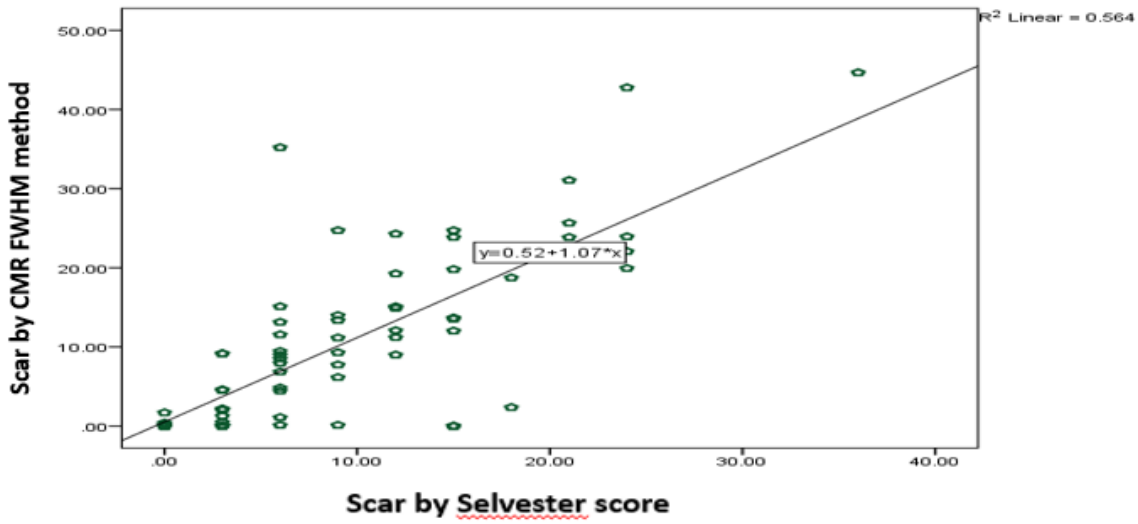


Fig-19. Correlation between FWHM and Selvester score

Bland Altman agreement analysis

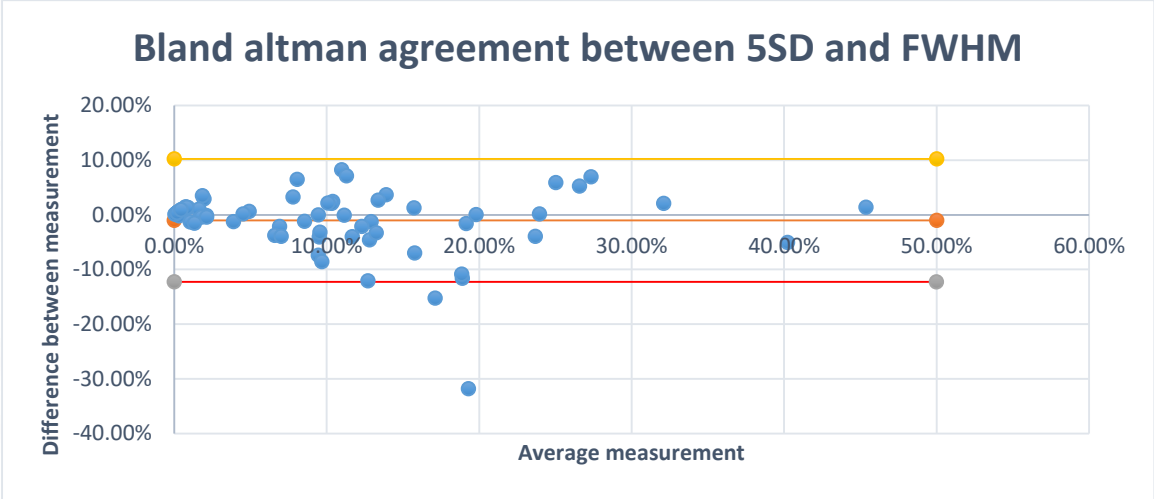


Fig-20. Average of the difference of observations between 5SD and FWHM is -1.02% with 1.96SD range of 10.24% to -12.29%.Only few observation average lies outside the range on the lower side suggests overestimation of scar by FWHM method.

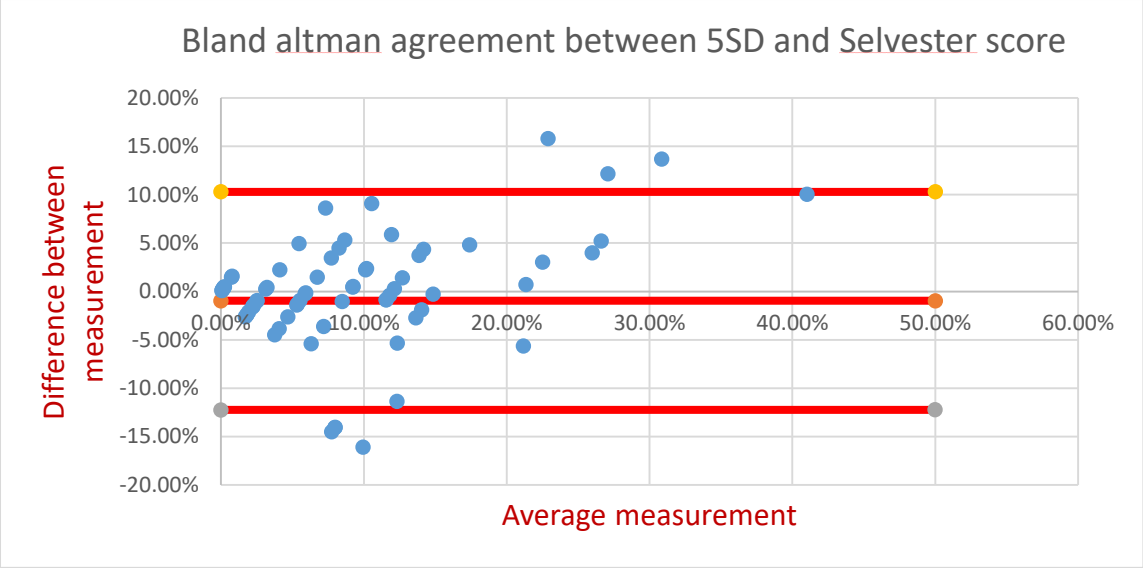


Fig 21. Average of the difference of observations between 5SD and Selvester score is -0.97% with 1.96SD range of 10.30% to -12.25%.Only few observation average lies outside the range and scattered all over suggestive of good agreement without consistent bias of any method.

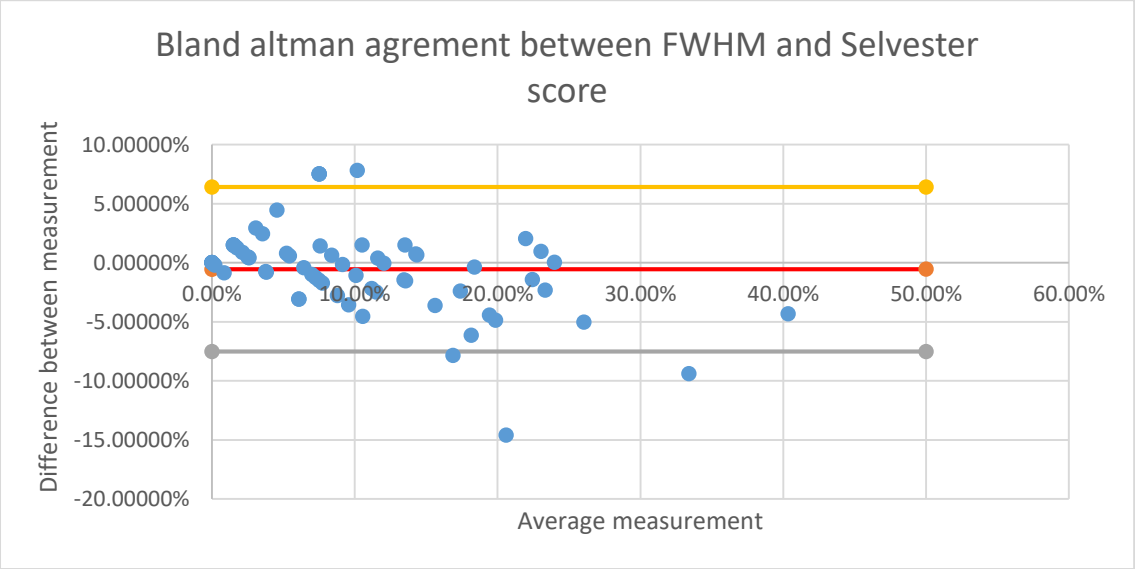


Fig 22- Average of the difference of observations between FWHM and Selvester score is -0.56% with 1.96SD range of 6.40% to -7.53%.Only few observation average lies outside the range and scattered all over suggestive of good agreement without consistent bias of any method.

Diagnostic ability of Selvester score in detection of scar in HCM patients:

For the calculation and diagnostic performance patients are divided into 2 groups whether scar is present (≥1% value by 5SD/FWHM methods and ≥3% by Selvester score) or absent(<1% value by 5SD/FWHM methods and 0 by Selvester method)

Scar by Selvester score	Scar by CMR 5SD method				Sensitivity	96.43
	Present	Absent			Specificity	50
Present	54	7	61		PPV	88.52
Absent	2	7	9		NPV	77.78
Total	56	14	N=70		Accuracy	87.1

Table-9. Sensitivity and specificity of Selvester score to detect scar diagnosed by 5SD method

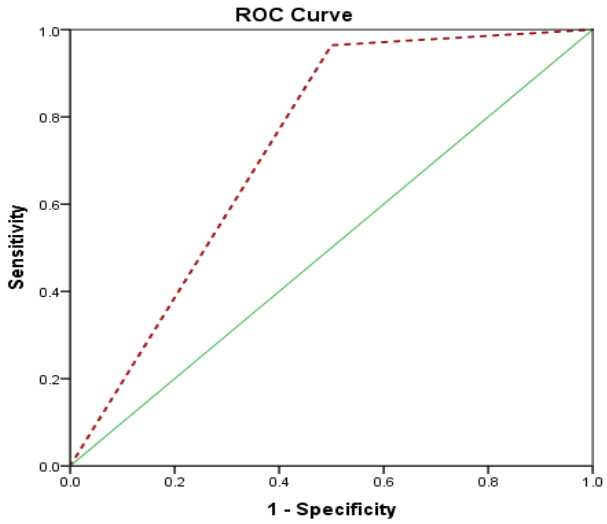


Fig-23. ROC for Selvester score to detect scar in comparison to 5SD method (AUC=0.732,p=0.008)

Scar by Selvester score	Scar by CMR FWHM method				Sensitivity	98.04
	Present	Absent			Specificity	42.11
Present	50	11	61		PPV	81.97
Absent	1	8	9		NPV	88.89
Total	51	19	N=70		Accuracy	82.9

Table-10.Sensitivity and specificity of Selvester score to detect scar diagnosed by FWHM method

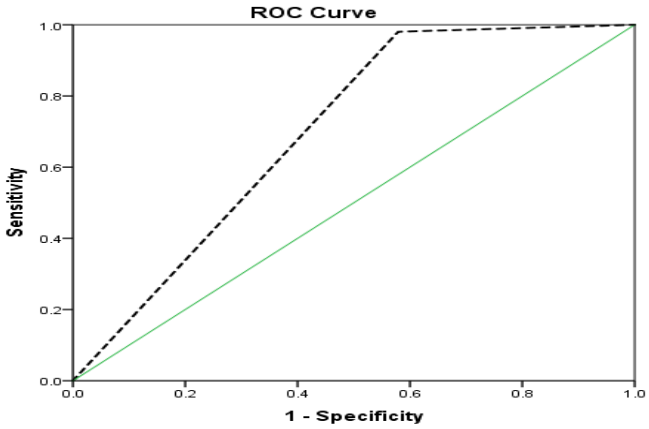


Fig –24.ROC for Selvester score to detect scar in comparison to FWHM method (AUC=0.701,p=0.0102)

There is good sensitivity of Selvester scoring method to detect presence of scar in HCM population. However specificity remains low.

Ability of Selvester score to detect high risk HCM patients (≥15% scar amount by CMR LGE):

Sensitivity, Specificity, PPV and NPV of Selvester scoring to detect ≥15% scar were calculated considering CMR LGE(5SD) as gold standard. It suggest Selvester scoring has high negative predictive value to identify true negative high risk patients.

High risk Scar by Selvester score	High risk Scar by CMR 5SD method					
	≥15%	<15%			Sensitivity	77%
					Specificity	84%
≥15%	10	9	19		PPV	53%
<15%	3	48	51		NPV	94%
Total	13	57	N=70		Accuracy	82.85%

Table-11. Sensitivity and specificity of Selvester score to detect high risk scar amount

One way analysis of variance (ANOVA) of 3 methods mean:

ANOVA test was performed to test the hypothesis and detect significant difference among the mean by 3 methods. Mean scar percentage values for 5SD, FWHM and Selvester score were 9.3%,10.3% and 9.2% respectively. There is no statistically significant difference among means by 3 methods of scar measurement as p value is >0.05 and null hypothesis accepted. The critical value of F at 95% probability level is much higher (3.07) than the observed value of F (0.29), which means that the null hypothesis is true.

	N	Mean	Std deviation	Std error		DF between 3 groups	2
CMR 5 SD	70	9.2696	9.8506	1.1774		Sum of squares	52.0531
CMR FWHM	70	10.297	10.7495	1.2848		Mean square	26.0266
Selvester score	70	9.2143	7.5294	0.8999		F Stat	0.29
						P Value	0.7486
						Critical F value	3.0718

Table-12 ANOVA test to detect difference among the mean by 3 methods

Association of scar burden and LVOT obstruction:

Analysis of this study suggest that 34 patients had significant LVOT obstruction defined as resting LVOT gradient >30mmHg or provoked gradient of >60 mmHg. However there is no significant difference in scar burden in presence or absent of LOT obstruction.

	Significant LVOT obstruction(N=34)	No LVOT obstruction(N=36)	P Value
Selvester score mean	10%	8%	0.274
5SD mean	9%	10%	0.673
FWHM mean	10%	11%	0.700

Table-13 Influence of scar burden on LVOT obstruction

DISCUSSION

This study aimed at demonstrating a correlation of scar measurement by LGE CMR and Selvester QRS score which was mainly used in the past for measurement of ischemic scar quantity. 70 patients were analysed as a part of the study. Mean age of study cohort was 49.7 years (Range-19 to 71 years, F=17).Mean scar percentage by 5SD, FWHM and Selvester score was 9.3%, 10.3% and 9.2% respectively. Modified QRS score strongly correlated with 5SD (r=0.813, p-0.0005) and FWHM (r=0.751, p=0.0005) CMR-LGE. Diagnostic ability of QRS score to detect ≥1% scar showed high sensitivity in comparison to 5SD (Sensitivity-96.43%, Specificity-50%) and FWHM (Sensitivity-98.04%, Specificity-42.11). One way ANOVA test suggest there is no statistically significant difference among the mean scar quantification by 3 methods(F stat-0.29,p=0.7486).Bland Altman analysis suggest good agreement with only few observations lie outside 1.96SD range without consistent bias of any method. Sub data analysis suggest that patients with NSVT on Holter study had higher scar burden by all 3 methods (p, 0.005) in comparison to patients with Normal Holter study. This suggest scar act as substrate for arrhythmogenesis.

Currently CMR LGE has been established standard for scar detection and quantification. Multiple studies already concluded regarding poor prognosis in relation to CMR scar burden in HCM patients. Scar burden of ≥15% of LV mass is considered high risk for SCD in HCM

patients. Scar burden can help in selecting patients who can get maximum benefit of ICD placement as a primary prophylaxis. However it is currently not included in the standard guidelines and considered as a risk modifier. Considering the future risk of SCD and limited availability of CMR especially in developing countries, there is a need for a widely available screening method to measure scar burden in these patients.

Sensitivity of technique

Only few studies are available where Selvester score was compared with other methods of scar quantification. Most of the studies available have analysed Selvester score in ischemic cardiomyopathy and very few studies have included non-ischemic aetiologies. Strauss et al has compared QRS scoring with CMR in 62 patients of ischemic or non-ischemic dilated cardiomyopathy with LVEF<35% prior to placement of ICD for primary prevention of SCD. They showed correlation of r=0.74, (P<0.0001) between CMR and Selvester scoring. They concluded that QRS scores identify and quantify scar in ischemic and non-ischemic cardiomyopathy patients despite ECG confounders. Higher QRS-estimated scar size is associated with increased arrhythmogenesis and warrants further study as a risk-stratifying tool (64). Similarly our cohort of HCM suggest good correlation (r=0.813, p-0.0005) between CMR 5SD and Selvester score and between CMR FWHM and Selvester score (r=0.751,p-0.0005).Also higher scar burden in patients with NSVT suggest scar act as substrate for arrhythmia. Strauss et al in a cohort of symptomatic Chaga's disease where they found correlation coefficient of r=0.69 between CMR LGE scar and QRS score. They concluded that, QRS score can be used as screening tool and may enhance risk stratification in patients with Chagas disease(65).Bignoto et al has published utility of QRS scoring in HCM cohort and compared with the scar quantification by delayed enhancement on cardiac CT. They found correlation of r=0.70, p<0.01. They concluded that Selvester QRS score provides reliable quantification of myocardial fibrosis and was well correlated with MDCT in patients with HCM (66).

According to our study Selvester score is showing high sensitivity (>95%) in detecting presence of scar in HCM cohort and can be used as a screening tool in this population. Although specificity remains low as CMR detection depends on signal difference between scar and normal myocardium and difficult to detect diffuse scar or interstitial fibrosis may not be detected by LGE but possibly identified by QRS score. Echo and Selvester score combined

can be used where CMR is not available to identify high risk population. However exact localisation of scar is not possible with Selvester score in comparison to CMR.

5SD versus FWHM

There is no consensus regarding the technique of quantification of late gadolinium enhancement (LGE) to quantify fibrosis. Moravsky et al has explored the relationship between CMR with LGE and histopathological parameters including interstitial fibrosis and replacement fibrosis (scar) in patients with HCM(51).They found Statistically significant correlations between CMR-LGE (at 2, 4, 5, 6, 10 SD and by the FWHM technique) analyse by pre-operative CMR, and both interstitial fibrosis and the combined interstitial and replacement fibrosis analysed from myectomy specimens. The strongest correlation was between combined interstitial and replacement fibrosis and CMR-LGE measured at 5 SD (r -0.78, $p< 0.0001$).

Spiewak et al has compared visual assessment of LGE and different thresholding techniques from 1SD to 6SD of signal intensity above normal myocardium as well as FWHM (50). They concluded that LGE quantification with the use of a threshold of 6SD above the mean SI of the remote myocardium provided the best agreement with visual assessment in patients with HCM. Although visual assessment is subjective with wide interobserver variability, they considered it as a reference method for comparison.

In our study, we found strong positive correlation between 5SD and FWHM methods of scar quantification r=0.848,p-0.0005.We conclude that both method can be used for scar estimation in HCM cohort. Although FWHM gives slightly higher value but statistically not significant. FWHM highly dependent on CNR of particular images as ROI is placed over the enhanced myocardium and ROI should include only enhancing area but occurrence of diffuse scar is more common in HCM patients which may include non-enhancing pixel in the ROI and overestimate scar.

Another study by Flett et al included 60 patients of different pathologies (AMI, CMI and HCM) who underwent CMR examination. LGE volume was quantified using the 7 techniques include manual quantification, thresholding by 2, 3, 4, 5, or 6 SDs above remote myocardium, and the full width at half maximum (FWHM) technique. They concluded that regardless of

the disease under study, the FWHM technique for LGE quantification gives LGE volume mean results similar to manual quantification and is statistically the most reproducible (52).

Mean scar percentage by 5SD, FWHM and Selvester score was 9.3%, 10.3% and 9.2% respectively. ANOVA test was performed to detect difference among the mean of 3 methods .Result suggest there was no statistically significant difference between means of scar percentage measured by 3 methods. This suggest Selvester score can be used reliably as a screening method or when CMR is contraindicated or during follow up cases.

Sub analysis in our study suggest there is significantly higher scar burden in patients with Abnormal Holter study defined as Non-sustained ventricular tachycardia(at least 3 runs) with ≥10 beats & ≥ 200 bpm when compared to patients with normal Holter study. Mean scar value in Abnormal Holter group was 18.42%, 17.43% and 23.59% by Selvester score,5SD and FWHM methods respectively.

Analysis about Selvester score to identify high risk HCM patients which is defined conventionally as ≥15% scar burden by CMR LGE suggest that it has high negative predictive value to detect high risk patients in comparison to 5SD CMR LGE method. This also favours use of Selvester scoring as a screening tool.

LVOT obstruction is a common finding in HCM which may be attributable to many factors like mitral leaflet length, systolic anterior motion of mitral leaflet, morphological abnormalities of valve, asymmetric septal hypertrophy. However there is no study regarding influence of scar on presence of LVOT obstruction. We calculated mean scar value in presence (resting gradient <30 or provoked gradient <60) and absence of LVOT obstruction (Resting >30 or provoked >60 mm hg) measured during catheterisation study. Analysis suggest that there is no statistical significant difference in scar burden in presence or absence of LVOT obstruction.

Selvester score is in multiple of 3 so using linear correlation equation y=0.43+1.06x (where y=predicted LGE by CMR method and x=Scar amount by Selvester method) we can predict CMR scar burden.

Although LV mass is higher in majority of HCM patients, it may be within normal range in up to 20% of the patients as described by Olivotto (74). They concluded A markedly increased LV mass (>91 g/m2 in men and >69 g/m2 in women) index proved to be more sensitive with regard to HCM-related death. In females average indexed LV mass was 85.68 gm/m2 (±21.7) .In males indexed LV mass was 94.72 gm/m2(±25.58).Till now none of the guideline has included indexed LV mass to predict SCD or to categorise high risk HCM patient. Average measurement of maximal LV wall thickness during end diastolic phase in this cohort was 20.1 mm(± 4.3mm).Only 4 patients has wall thickness >30 mm. maximal wall thickness >30 mm was considered more specific to predict future HCM related death. There is poor correlation between LV mass and maximum LV wall thickness.

Case 1

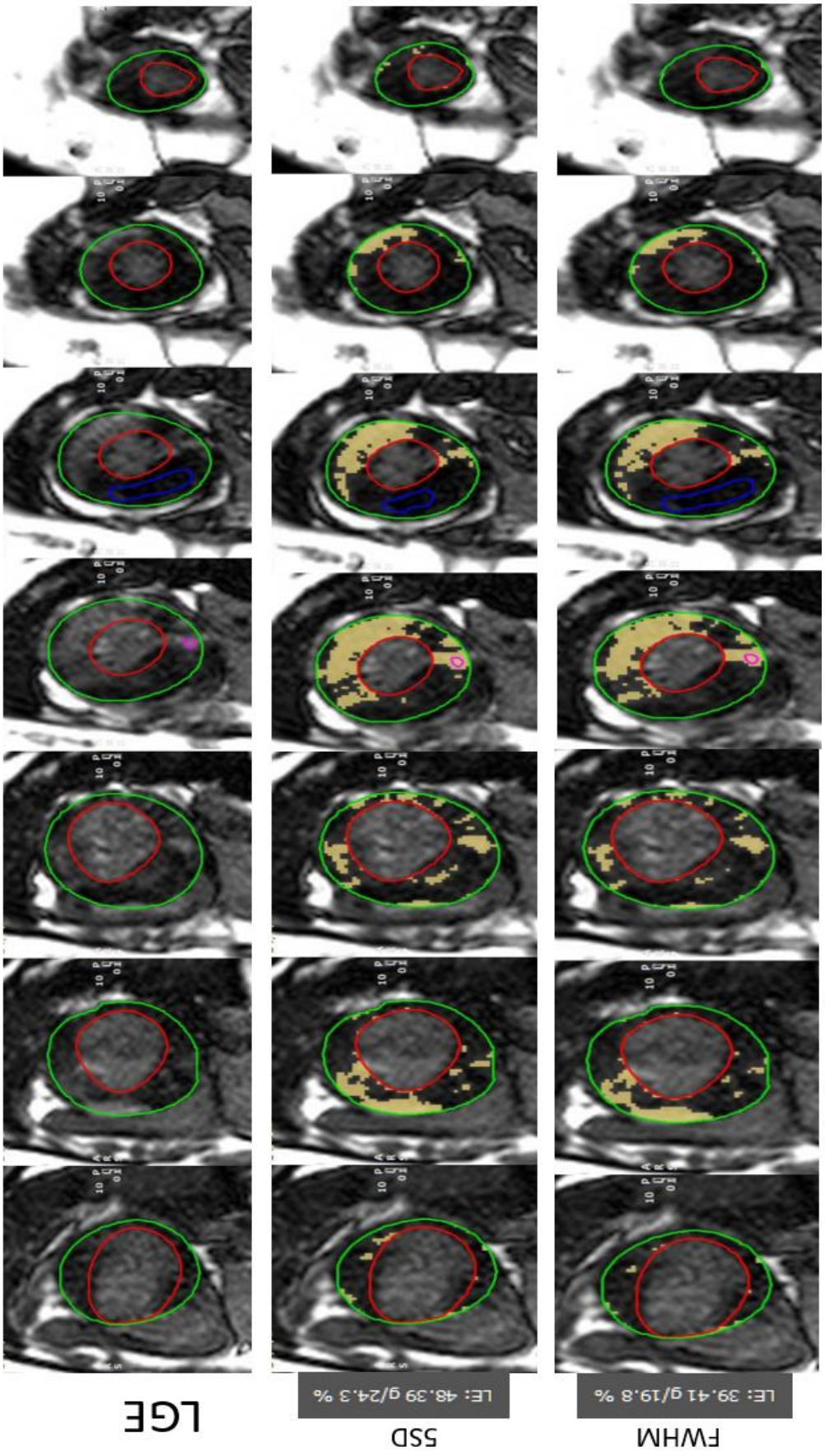
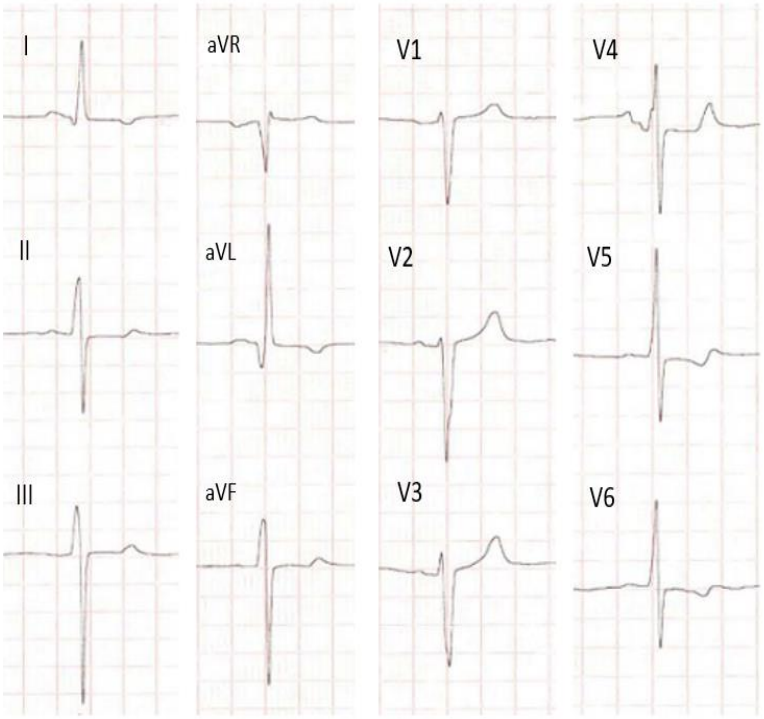


Fig-25.SA LGE images show enhancing myocardium which was quantified using 5SD(Blue ROI in normal myocardium) and FWHM (Pink in Enhanced myocardium).Scar burden was 24.3% and 19.8 %



V1-Negative deflection
QRSd-110ms
Axis: -50
Confounding is LAFB.

Lead I: Q ≥ 30ms(1 score)
AVL: Q ≥ 40ms (1 score)
V2: R ≤ 0.1 mv (1 score)
V3: R ≤ 20ms (1 score)
V4: R/S ≤ 1 (1 score)
V5: R/S ≤ 1.5 (1 score)
V6: R/S ≤ 2 (1 score)
Total score-7
Scar burden-21%

Case 2:

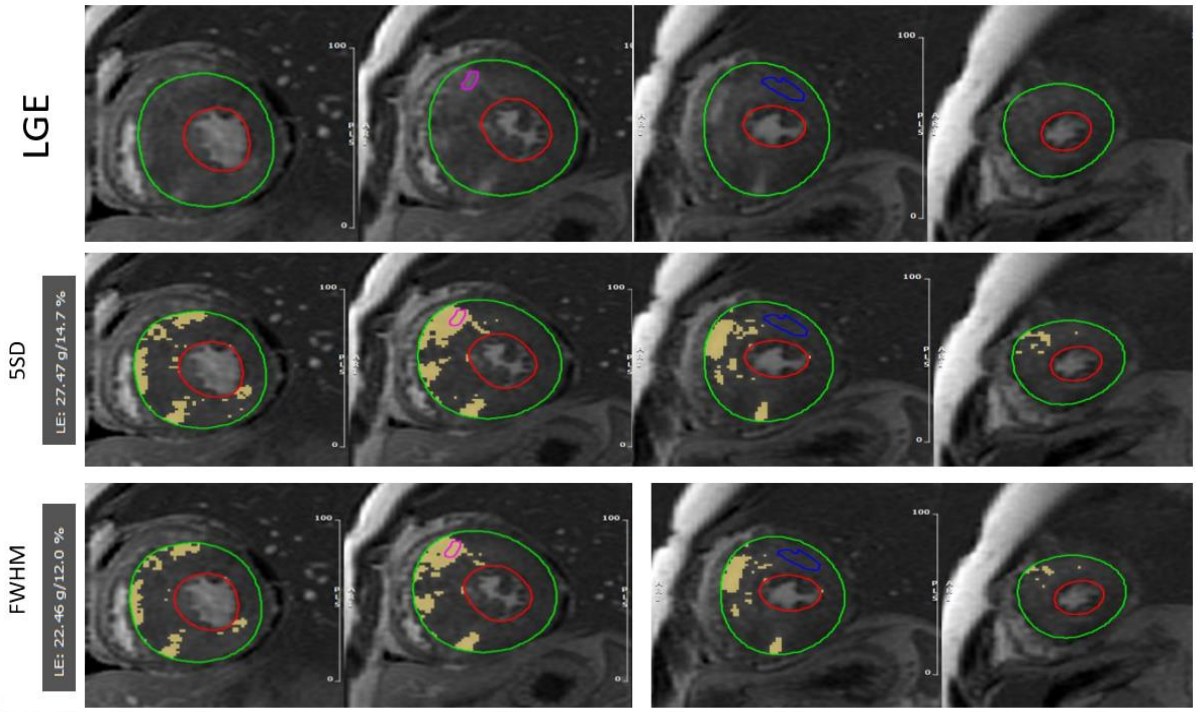
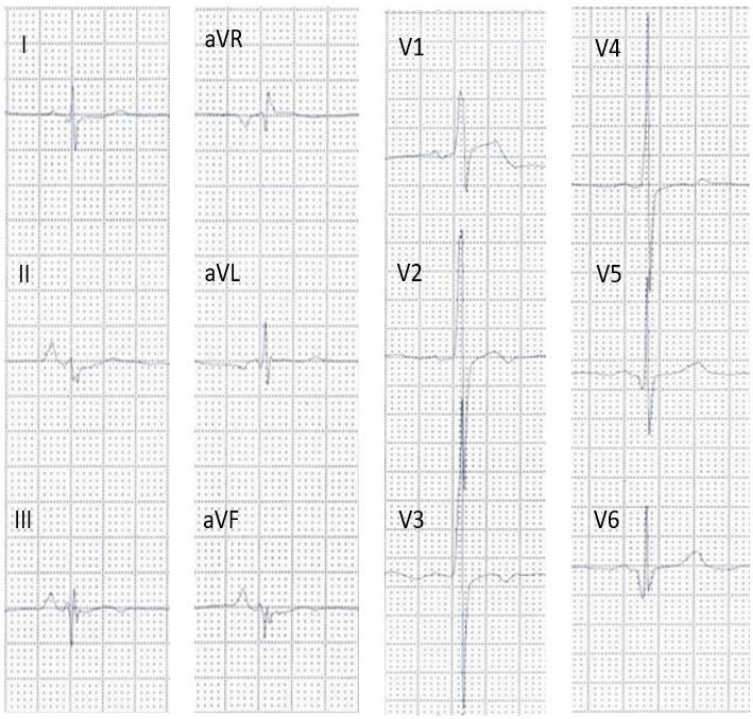


Fig-26.SA LGE images show enhancing myocardium which was quantified using 5SD (Blue ROI in normal myocardium) and FWHM (Pink in Enhanced myocardium).Scar burden was 12% and 14.7 % respectively with 5SD and FWHM methods. Selvester score was 4 (12% scar) after LAFB as a confounder.



V1-Positive deflection
QRSd-110 ms
Axis: -90 degree
Confounding is LAFB
Lead I: Q ≥ 30ms (1 score)
V5: Q ≥ 30ms (1 score)
V6: Q ≥ 30ms (1 score)
R/Q ≤ 3 (1 score)
Total score-4
Scar burden-12%

Case 3

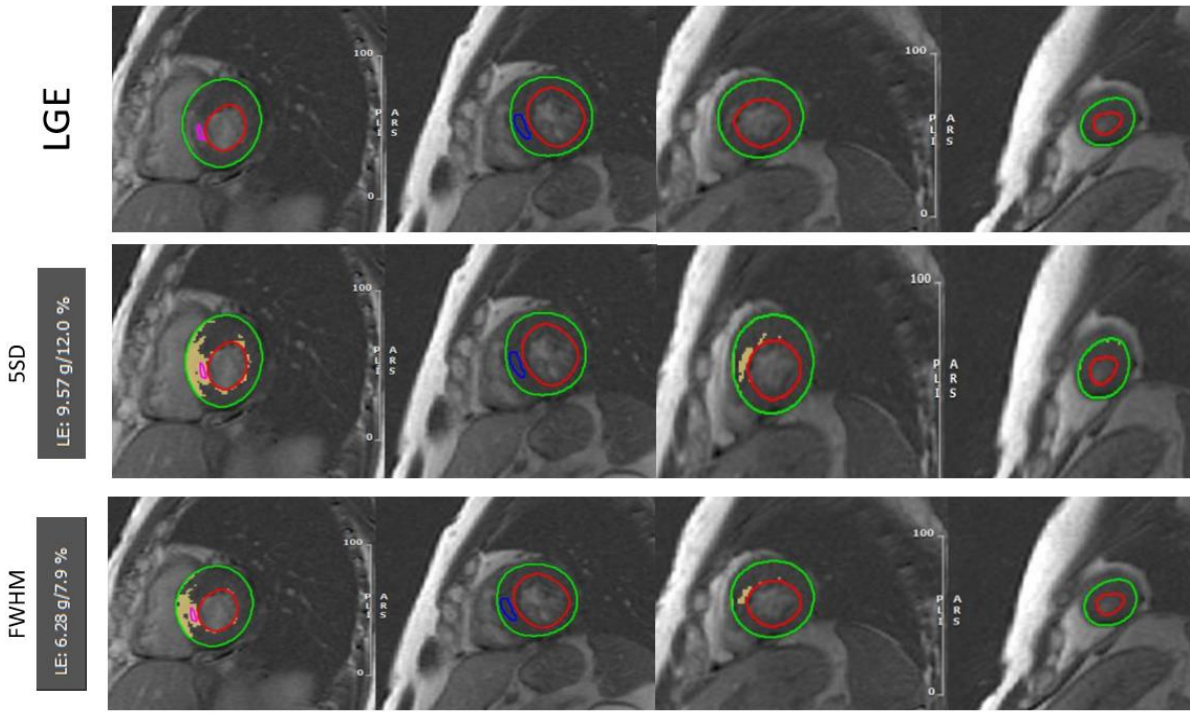
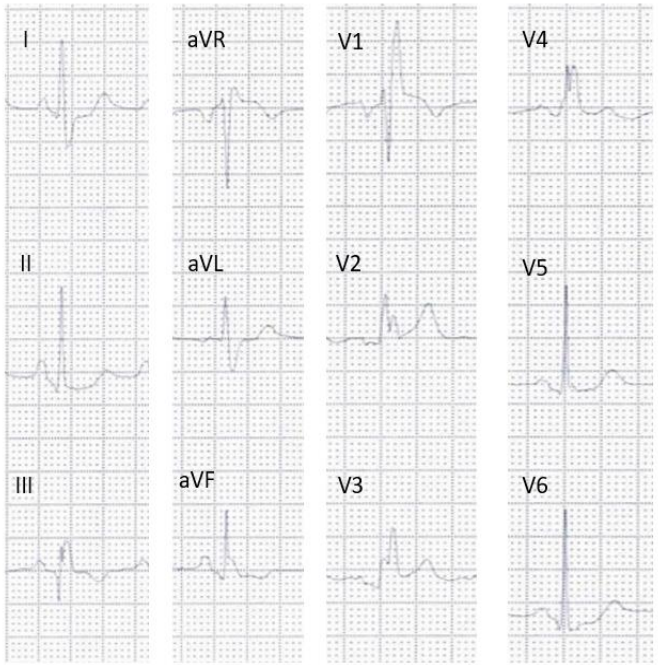


Fig-27.SA LGE images show enhancing myocardium which was quantified using 5SD (Blue ROI in normal myocardium) and FWHM (Pink in Enhanced myocardium). Scar burden was 12% and 7.9 % respectively with 5SD and FWHM methods. Selvester score was 5 (15% scar) after RBBB as a confounder.



V1 deflection:Positive rSR'
QRSd-130ms
Axis: +65
Confounder is RBBB
Lead I: Q ≥ 30ms(1 score)
Lead II: Q ≥ 30ms(1 score)
AVF : Q ≥ 40ms(2 score)
V6 : Q ≥ 30ms(1 score)
Total score-5
Scar burden 15%

Case 4

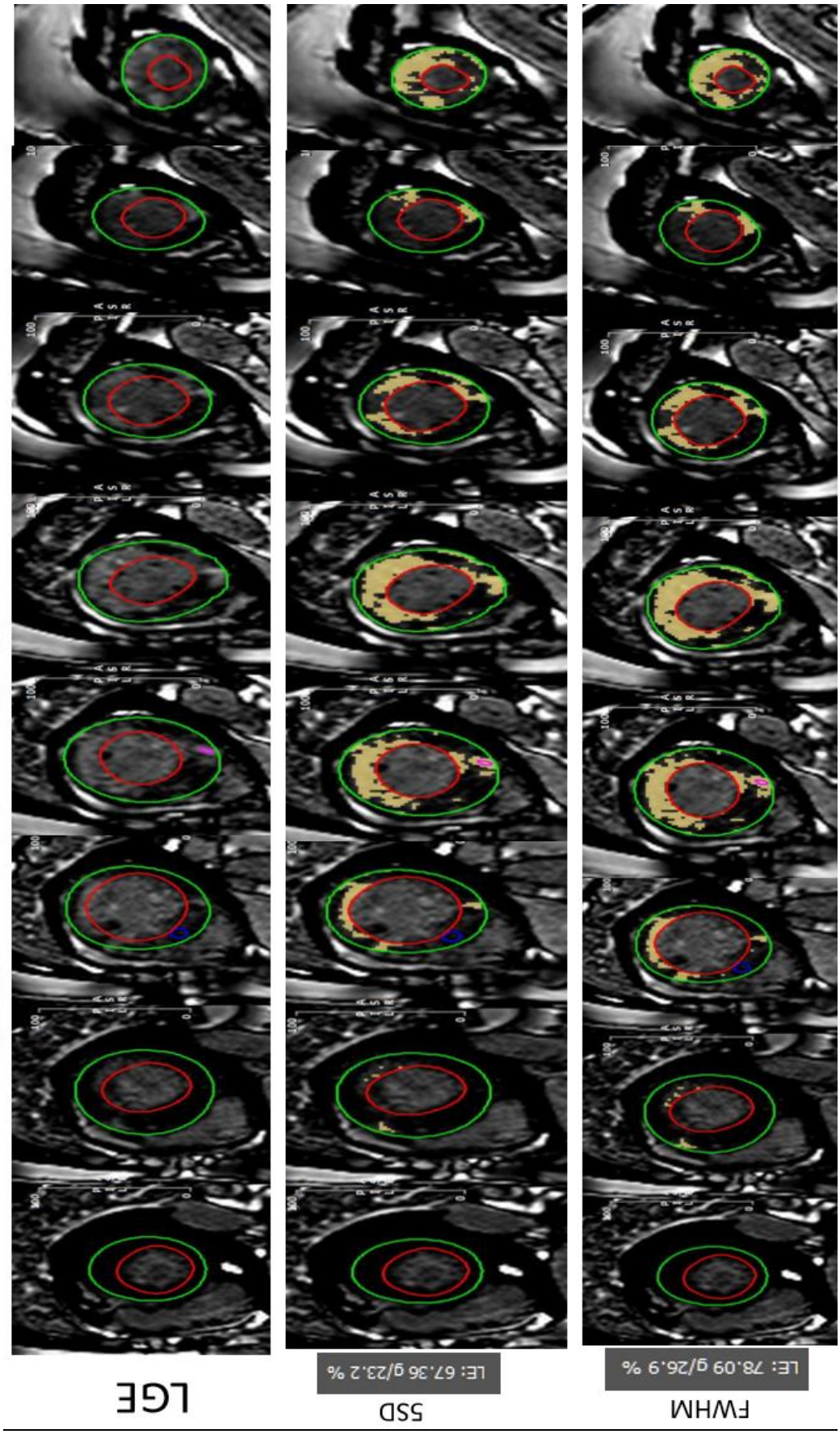
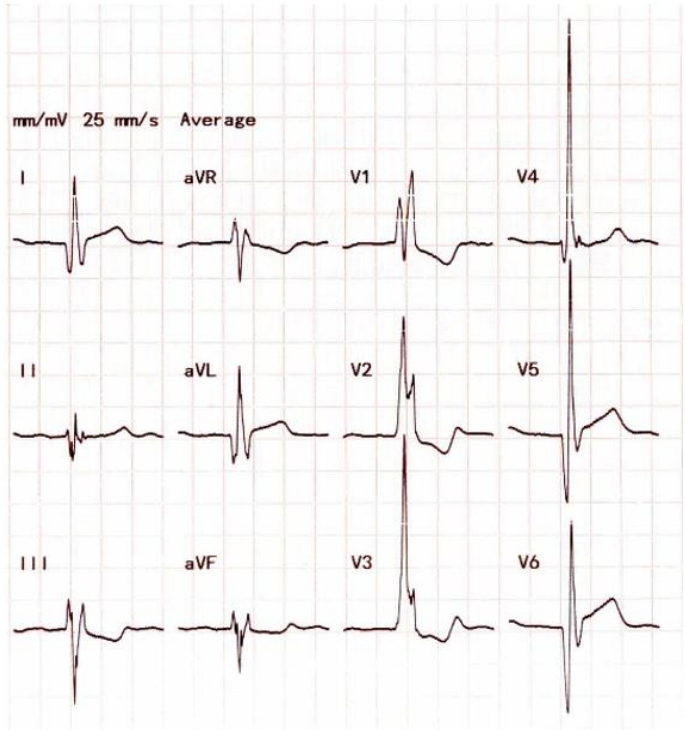


Fig-28.SA LGE images show enhancing myocardium which was quantified using 5SD(Blue ROI in normal myocardium) and FWHM (Pink in Enhanced myocardium).Scar burden was 23.2% and 26.9 % respectively with 5SD and FWHM methods. Selvester score was 7(21% scar) after RBBB as a confounder.



V1-Positive deflection-RSR'
QRSd-140 ms
QRS axis: -30
Confounding is RBBB
Lead I : Q ≥ 30ms(1 score)
Lead II : Q ≥ 40ms (2 score)
AVL : Q ≥ 30ms(1 score)
V4 : Q ≥ 20ms(1 score)
V5 : Q ≥ 30ms(1 score)
V6 : Q ≥ 30ms(1 Score)
R/S ≤ 3 (1 score)
Total score - 8
Scar burden 24%

LIMITATION

The current study had some limitations in that it was an observational and descriptive study which is not followed for events.

Limitations of LGE CMRI include that enhanced myocardial fibrotic tissue is defined on the basis of the difference in signal intensity between fibrotic and normal myocardium and this difference generates the image contrast. Diffuse fibrosis can go undetected when no reference identifiable normal myocardium. Detection and drawing of ROI for normal myocardium is subjective which adds the inter-observer variability. LGE may not detect interstitial type of fibrosis.

Limitations of QRS Scoring include ECGs were not digital in this study. It is possible that beat-to-beat variation may lead to different numbers of points to be assigned to a lead depending on which beat is evaluated Limitations of beat-to-beat variability, poor-quality paper ECGs and the increasing complexity of the QRS score criteria can be improved by digital ECGs and automated versions of QRS scoring, which could allow widespread use in clinical practice with less inter-observer variability during future studies. ECG can determine presence or absence of myocardial scar in HCM cohort with quantification. However exact localisation of scar may be difficult. Study by Wieslander et al(75) suggest it is possible to localise using ECG scoring, however they included only patients with LBBB. Further study regarding this aspect may be helpful.

CONCLUSIONS:

In conclusion, the Selvester QRS score facilitates quantitative measurement of the fibrotic burden in patients with HCM, and its findings were correlated strongly with those of LGE CMR methods. Since the Amount of scar has been associated with prediction of SCD and progression to heart failure, the use of an ECG technique such as the Selvester QRS score may be an alternative tool to quantitatively assess fibrosis in patients with HCM. The inexpensive and widely available 12-lead ECG could potentially be used as a screening tool to quantify scar and identify high risk subgroup of HCM patients indirectly. It can be used alternatively when CMR is contraindicated or not available as well as during clinical follow up. Using linear correlation between CMR scar and Selvester score, one can predict CMR scar from Selvester score. Future research is needed regarding utility of QRS score to differentiate high risk from low risk HCM patients. Further study is needed to determine if the QRS score might have a clinical impact on detecting fibrosis and predicting mortality.

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A	S	C	D	H	L	P	Sy	Fh	Hol	EF	5SD	FWH	SS	Con	AM	IM	MWT	LVG
71	M	I	No	No	No	Yes	No	No	Normal	41.95%	46.05%	44.67%	36%	LBBB	103.58	58.6	18.86 mm	0
52	M	I	Yes	No	No	No	No	Yes	Normal	56%	0.97%	0%	15%	LAFB	118.83	63	15 mm	0
53	M	III	Yes	Yes	No	Yes	Yes	No	NSVT	64.41%	15.74%	12.08%	12%	LAFB	111.5	67.65	18.43 mm	0
29	M	II	No	No	No	Yes	No	Yes	Normal	66.56%	5.39%	13.99%	9%	LAFB	218.54	127	22.1 mm	0
30	F	II	No	No	No	Yes	Yes	Yes	Normal	57.12%	24.04%	23.86%	21%	LAFB	98.14	59.18	19.81 mm	0
50	M	II	Yes	No	No	Yes	Yes	No	Normal	57%	33.15%	31.06%	21%	LAFB	139.3	91	18 mm	0
64	M	II	No	No	No	No	No	Yes	NSVT	57.64%	37.69%	42.77%	24%	LAFB	131	99	23 mm	10
23	M	II	No	No	No	No	No	No	Normal	74.36%	14.71%	12.03%	15%	LAFB	229.07	132.72	32.5 mm	64
31	F	II	No	No	No	No	Yes	No	Normal	68.44%	19.81%	19.80%	15%	LAFB	193.14	136.14	22.29 mm	90
33	M	II	No	No	No	No	Yes	No	Normal	81.79%	11.31%	4.83%	6%	LAFB	129.32	74.31	22.13 mm	120
36	M	II	No	No	No	No	Yes	Yes	Normal	55.43%	14.86%	7.75%	9%	LAFB	212.2	99.03	31.3 mm	65(P)
22	F	II	No	No	No	Yes	Yes	No	Normal	81.10%	9.67%	13.68%	15%	LAFB	189.58	109.32	24.1 mm	65(P)
48	M	I	No	Yes	No	Yes	No	Yes	NSVT	59.35%	1.47%	0.08%	3%	LBBB	190.97	113.98	18.29 mm	0
59	M	II	Yes	No	No	No	No	No	Normal	73.21%	0.37%	0%	0%	LVH	150.99	84.3	18.26 mm	0
61	M	II	No	Yes	No	No	Yes	No	Normal	68.66%	2.06%	2.19%	3%	LVH	168.73	93.91	22.59 mm	0
48	M	II	No	No	No	No	No	Yes	Normal	71.07%	11.16%	9%	12%	LVH	92.09	66.62	15.43 mm	0
53	M	II	No	Yes	No	Yes	No	No	Normal	75.42%	7.94%	9.14%	3%	LVH	143.01	76.39	16.7 mm	0
49	M	II	No	Yes	No	No	No	Yes	Normal	64.25%	11.63%	9.18%	3%	LVH	263.25	141.13	30.3 mm	0
50	M	II	No	No	No	No	Yes	Yes	NSVT	75.50%	3.37%	35.21%	6%	LVH	112.82	70.71	17.63 mm	0
67	M	III	No	No	No	Yes	Yes	No	Normal	71.68%	1.40%	0.10%	3%	LVH	156.71	86.71	19.55 mm	10
32	M	III	No	No	No	No	Yes	No	NSVT	75.02%	9.45%	9.45%	6%	LVH	250.1	124.84	23.23 mm	10
55	M	III	No	No	No	Yes	Yes	No	Normal	75.45%	0.90%	0%	3%	LVH	166.71	94.43	24.16 mm	16
61	F	II	No	No	No	No	No	No	Normal	76.16%	0.24%	0.41%	0%	LVH	110.3	72.8	16.33 mm	16
35	F	III	No	No	No	Yes	No	No	Normal	76.90%	7.96%	11.16%	9%	LVH	130.6	80.1	16 mm	20
64	M	II	No	Yes	No	Yes	No	No	NSVT	75.86%	0.16%	0%	0%	LVH	188	102	21.22 mm	35
51	M	II	No	No	No	Yes	No	Yes	Normal	72.70%	0.55%	2.11%	3%	LVH	208.39	109.49	18.59 mm	38
48	M	II	No	No	No	Yes	Yes	No	NSVT	72.86%	13.09%	24.72%	15%	LVH	226.28	117.44	25.57 mm	50
42	M	II	No	No	No	Yes	No	No	Normal	68.91%	5.23%	4.61%	3%	LVH	135.47	67.82	20.48 mm	51
55	M	III	No	Yes	No	No	No	No	Normal	63.20%	5.84%	7.97%	6%	LVH	298	128	25.43 mm	64
43	M	III	No	No	No	Yes	Yes	No	Normal	82.44%	10.50%	15.11%	6%	LVH	180.36	106.79	21.55 mm	70
45	M	II	No	No	No	No	Yes	No	Normal	67.88%	1.56%	2%	3%	LVH	238.26	150.09	22.86 mm	80
19	M	III	No	No	No	No	Yes	No	Normal	63.05%	5.76%	13.14%	6%	LVH	321.9	143.17	25.69 mm	90
36	F	II	No	No	No	Yes	No	Yes	NSVT	73.14%	0.93%	0%	15%	LVH	117.49	82.99	17.69 mm	96
40	M	II	No	Yes	No	No	Yes	No	Normal	72.01%	3.60%	0.12%	9%	LVH	117.12	62.53	15.12 mm	100
47	M	II	No	No	No	No	Yes	No	Normal	63.89%	0.40%	1.70%	0%	LVH	176.75	97.89	17.8 mm	100
37	M	III	No	No	No	Yes	Yes	Yes	Normal	77.53%	16.35%	15.10%	12%	LVH	205.76	119.21	24.28 mm	120
55	F	II	Yes	Yes	No	Yes	Yes	No	Normal	78.57%	9.44%	6.16%	9%	LVH	197	119	26.78 mm	160
62	F	II	No	Yes	No	No	No	No	Normal	74.91%	1.53%	0.12%	6%	LVH	122.55	76.76	18.58mm	120(P)
53	M	II	No	No	No	Yes	No	No	Normal	66.98%	1.90%	2.36%	18%	LVH	165.89	112.23	16.88 mm	65(P)
32	M	II	No	No	No	No	Yes	No	Normal	68.26%	27.98%	22.07%	24%	LVH	117.23	70.3	16.09 mm	65(P)
56	M	II	No	No	No	No	Yes	No	Normal	75.07%	2.15%	1.10%	6%	LVH	110.6	90.86	15.38 mm	90(P)
70	F	III	No	No	No	No	No	No	Normal	71.58%	0.38%	0%	3%	NC	110.13	79.76	15.5 mm	0
65	F	II	No	Yes	No	Yes	Yes	No	Normal	82.17%	4.61%	4.44%	6%	NC	138.93	87.87	21 mm	0
57	M	II	No	No	No	No	Yes	No	NSVT	65.32%	18.35%	19.94%	24%	NC	99.92	62.93	16.8 mm	0
47	M	III	No	No	No	No	No	No	Normal	81.79%	4.71%	8.50%	6%	NC	106.45	65.22	15.44 mm	60

41	M	II	No	No	No	Yes	Yes	No	Normal	75.51%	11.37%	9.29%	9%	NC	164.66	93.74	23.16 mm	74
46	F	III	No	Yes	No	Yes	No	No	Normal	60.17%	0.48%	0%	15%	NC	131.41	77.99	22.78 mm	80(P)
57	M	III	No	Yes	No	No	No	No	Normal	66.38%	9.51%	24.73%	9%	RBBB	232.48	132.26	20.1 mm	80
35	M	II	No	No	No	No	Yes	No	Normal	76.41%	12.27%	19.26%	12%	RBBB + LAFB	163.69	99.01	23.61 mm	90
42	M	II	No	No	No	No	Yes	Yes	Normal	74.84%	11.60%	14.90%	12%	RBBB + LAFB	213.48	135	23.21 mm	94
69	M	II	No	Yes	Yes	Yes	Yes	No	NSVT	48.50%	13.41%	24.29%	12%	LAFB	159.33	95.22	17.7 mm	0
60	M	II	No	Yes	Yes	Yes	yes	No	Normal	76.71%	0.33%	0%	0%	LVH	102.29	62.84	15.3 mm	0
63	F	II	No	Yes	Yes	No	No	No	Normal	76.21%	1.47%	0.01%	0%	LVH	96.67	56.99	15.39 mm	0
58	M	II	Yes	Yes	Yes	Yes	Yes	No	NSVT	67.49%	3.42%	0.49%	3%	LVH	118.43	63.44	16.29 mm	0
65	M	II	No	Yes	Yes	No	No	No	Normal	70.54%	3.24%	4.52%	3%	LVH	137.39	72.86	16.09 mm	0
62	M	II	No	Yes	Yes	Yes	No	No	Normal	69.66%	5.05%	8.98%	6%	LVH	136.38	91.56	15.94 mm	0
54	M	II	No	No	Yes	Yes	yes	No	Normal	57.72%	11.11%	11.21%	12%	LVH	194.02	108.3	21.24 mm	0
58	M	I	No	No	Yes	No	No	No	Normal	58.71%	7.47%	11.56%	6%	LVH	145.74	77.16	17.34 mm	0
57	F	II	No	Yes	Yes	Yes	Yes	No	Normal	74.50%	12.28%	13.54%	15%	LVH	114.81	63.43	18.78mm	0
52	M	II	Yes	Yes	Yes	Yes	No	No	Normal	72.11%	30.81%	23.87%	15%	LVH	220	123	30.5 mm	0
61	F	III	Yes	Yes	Yes	No	Yes	No	NSVT	80.35%	0.64%	0%	3%	LVH	123.38	72.88	16.35 mm	6
53	F	III	No	Yes	Yes	Yes	No	No	Normal	70%	2%	1.28%	3%	LVH	158	110	18.5 mm	40
45	F	II	No	No	Yes	No	Yes	No	NSVT	79.75%	29.21%	23.94%	24%	LVH	164.18	94.73	23.14 mm	45
32	M	II	No	Yes	Yes	Yes	Yes	Yes	NSVT	70.90%	21.70%	26%	21%	LVH	181.21	111.3	26.63 mm	50
60	M	III	No	Yes	Yes	No	Yes	Yes	Normal	61.74%	0.49%	0%	0%	LVH	189.54	107.83	18.62 mm	100(P)
48	F	II	No	Yes	Yes	Yes	No	No	Normal	67.69%	6.65%	18.74%	18%	LVH	113.44	76.73	21.90 mm	130(P)
71	M	II	No	No	Yes	Yes	No	No	Normal	76.95%	11.24%	13.37%	9%	LVH	121.19	76.2	15.1 mm	70(P)
65	M	III	No	Yes	Yes	Yes	No	Yes	Normal	76.41%	0.10%	0%	0%	NC	108.02	60.73	16.61 mm	0
43	M	II	Yes	Yes	Yes	Yes	No	No	Normal	59.06%	1.56%	0.24%	0%	NC	133.5	64.17	15.88 mm	0
46	M	II	Yes	Yes	Yes	Yes	Yes	Yes	Normal	72.25%	15.10%	6.86%	6%	NC	126.25	74.27	15.26 mm	0

Key to master chart

A-Age

S-Sex

C-Clinical presentation(NYHA class)

D-Diabetes mellitus

H-HTN

L-Dyslipidemia

P-Palpitation

Sy -Syncope

Fh -Family history

Hol -Holter

EF-Ejection fraction measured by CMR

5SD-Scar quantification by 5SD method

FWH-Scar quantification by FWHM method

SS-Scar quantification by Selvester score

Con-Confounding factor

AM-Absolute LV mass in Gm

IM-Indexed LV mass in gm/m2

MWT-Maximum LV wall thickness

LVG-LVOT gradient measured by Catheterisation study

Annexures

Selvester scoring sheet

Patient ID _____ QRS duration _____ Amplitude adjust _____
(↑1%/yr age 20-54; ↓1%/yr >55 yrs; ↓10% for females

Age & gender _____ QRS axis _____ Duration adjust _____ RAO(**, ***)Yes/No
(↓ 10% for females)

Lead	RBBB Criteria	Pts	LAFB Criteria	Pts	LAFB + RBBB Criteria	Pts	LVH Criteria	Pts	No Confounders Criteria	Pts
I	Q ≥ 30 ms	1	Q ≥ 30 ms	1	Q ≥ 30 ms	1	Q ≥ 30 ms	1	Q ≥ 30 ms	1
	R/Q ≤ 1	1	R/Q ≤ 1	1	R/Q ≤ 1	1	R/Q ≤ 1	1	R/Q ≤ 1	1
	R ≤ 0.2 mV		R ≤ 0.2 mV		R ≤ 0.2 mV		R ≤ 0.2 mV		R ≤ 0.2 mV	
II	Q ≥ 40 ms	2	Q ≥ 40 ms	2	Q ≥ 40 ms	2	Q ≥ 40 ms	2	Q ≥ 40 ms	2
	Q ≥ 30 ms	1	Q ≥ 30 ms	1	Q ≥ 30 ms	1	Q ≥ 30 ms	1	Q ≥ 30 ms	1
aVL	Q ≥ 30 ms	1	Q ≥ 40 ms	1	Q ≥ 40 ms	1	Q ≥ 40 ms	1	Q ≥ 30 ms	1
	R/Q ≤ 1	1	R/Q ≤ 1	1	R/Q ≤ 1	1	R/Q ≤ 1	1	R/Q ≤ 1	1
aVF	Q ≥ 50 ms	3	Q ≥ 50 ms	3	Q ≥ 50 ms	3	Q ≥ 60 ms	3	Q ≥ 50 ms	3
	Q ≥ 40 ms	2	Q ≥ 40 ms	2	Q ≥ 40 ms	2	Q ≥ 50 ms	2	Q ≥ 40 ms	2
	Q ≥ 30 ms	1	Q ≥ 30 ms	1	Q ≥ 30 ms	1	Q ≥ 40 ms	1	Q ≥ 30 ms	1
	R/Q ≤ 1	2	R/Q ≤ 1	2	R/Q ≤ 1	2	R/Q ≤ 1	2	R/Q ≤ 1	2
	R/Q ≤ 2	1	R/Q ≤ 2	1	R/Q ≤ 2	1	R/Q ≤ 2	1	R/Q ≤ 2	1
V1 Ant.	Q ≥ 50 ms	2			Q ≥ 50 ms	2	any QR			
	any Q	1	any QR	1	any Q	1	(or any Q if *)	1	any Q	1
	Init R ≤ 20 ms						NtchInit40			
V1 Post.**			R/S ≥ 1	1		1	R/S ≥ 1	1	R/S ≥ 1	1
	Init R ≥ 60 ms	2	R ≥ 50 ms	2	Init R ≥ 60 ms	2	R ≥ 50 ms	2	R ≥ 50 ms	2
	Init R ≥ 1.5 mV		R ≥ 1mV		Init R ≥ 1.5 mV		R ≥ 1mV		R ≥ 1mV	
	Init R ≥ 50 ms	1	R ≥ 40 ms	1	Init R ≥ 50 ms	1	R ≥ 40 ms	1	R ≥ 40 ms	1
	Init R ≥ 1.0 mV		R ≥ 0.7 mV		Init R ≥ 1.0 mV		R ≥ 0.7 mV		R ≥ 0.7 mV	
			Q≤0.2&S≤0.2mV	1			Q≤0.2&S≤0.2 mV	1	Q≤0.2&S≤0.2mV	1
V2 Ant.	Q ≥ 50 ms	2			Q ≥ 50 ms	2				
	any Q	1	any QR	1	any Q	1	any QR	1	any Q	1
	R ≤ 10 ms		R ≤ 10 ms		R ≤ 10 ms		(or any Q if *)		R ≤ 10 ms	
	R ≤ 0.1mV		R ≤ 0.1mV		R ≤ 0.1mV		NtchInit40		R ≤ 0.1mV	
V2 Post.**			R/S ≥ 1.5	1			R/S ≥ 1.5	1	R/S ≥ 1.5	1
	Init R ≥ 70 ms	2	R ≥ 60 ms	2	Init R ≥ 70 ms	2	R ≥ 60 ms	2	R ≥ 60 ms	2
	Init R ≥ 2.5 mV		R ≥ 2 mV		Init R ≥ 2.5 mV		R ≥ 2 mV		R ≥ 2 mV	
	Init R ≥ 50 ms	1	R ≥ 50 ms	1	Init R ≥ 50 ms	1	R ≥ 50 ms	1	R ≥ 50 ms	1
	Init R ≥ 2.0 mV		R ≥ 1.5 mV		Init R ≥ 2.0 mV		R ≥ 1.5 mV		R ≥ 1.5 mV	
			Q≤0.3&S≤0.3mV	1			Q≤0.3&S≤0.3mV	1	Q≤0.3&S≤0.3mV	1
V3	Q ≥ 30 ms	2	Q ≥ 30 ms	2	Q ≥ 30 ms	2	QR& (Q ≥ 30 ms)	2	Q ≥ 30 ms	2
	R ≤ 10 ms		R ≤ 10 ms		R ≤ 10 ms		NtchInit40	1	R ≤ 10 ms	
	Q ≥ 20 ms	1	Q ≥ 20 ms	1	Q ≥ 20 ms	1	any QR		Q ≥ 20 ms	1
	R ≤ 20 ms		R ≤ 20 ms		R ≤ 20 ms		(or any Q if *)		R ≤ 20 ms	
V4	Q ≥ 20 ms	1	Q ≥ 20 ms	1	Q ≥ 20 ms	1	Q ≥ 20 ms	1	Q ≥ 20 ms	1
	R/Q ≤ 0.5	2	R/Q ≤ 0.5	2	R/Q ≤ 0.5	2	R/Q ≤ 0.5	2	R/Q ≤ 0.5	2
	R/S ≤ 0.5		R/S ≤ 0.5		R/S ≤ 0.5		R/S ≤ 0.5		R/S ≤ 0.5	
	R/Q ≤ 1	1	R/Q ≤ 1	1	R/Q ≤ 1	1	R/Q ≤ 1	1	R/Q ≤ 1	1
	R/S ≤ 1		R/S ≤ 1		R/S ≤ 1		R/S ≤ 1		R/S ≤ 1	
	R ≤ 0.5 mV		R ≤ 0.5 mV		R ≤ 0.5 mV		R ≤ 0.5 mV		R ≤ 0.5 mV	
	NtchInit40		NtchInit40		NtchInit40		NtchInit40		NtchInit40	
V5	Q ≥ 30 ms	1	Q ≥ 30 ms	1	Q ≥ 30 ms	1	Q ≥ 30 ms	1	Q ≥ 30 ms	1
	R/Q ≤ 1	2	R/Q ≤ 1	2	R/Q ≤ 1	2	R/Q ≤ 1	2	R/Q ≤ 1	2
	R/S ≤ 1		R/S ≤ 1		R/S ≤ 1		R/S ≤ 1		R/S ≤ 1	
	R/Q ≤ 2	1	R/Q ≤ 2	1	R/Q ≤ 2	1	R/Q ≤ 2	1	R/Q ≤ 2	1
	R/S ≤ 2		R/S ≤ 1.5		R/S ≤ 1.5		R/S ≤ 2		R/S ≤ 2	
	R ≤ 0.6 mV		R ≤ 0.6 mV		R ≤ 0.6 mV		R ≤ 0.6 mV		R ≤ 0.6 mV	
	NtchInit40		NtchInit40		NtchInit40		NtchInit40		NtchInit40	
V6	Q ≥ 30 ms	1	Q ≥ 30 ms	1	Q ≥ 30 ms	1	Q ≥ 30 ms	1	Q ≥ 30 ms	1
	R/Q ≤ 1	2	R/Q ≤ 1	2	R/Q ≤ 1	2	R/Q ≤ 1	2	R/Q ≤ 1	2
	R/S ≤ 1		R/S ≤ 1		R/S ≤ 1		R/S ≤ 1		R/S ≤ 1	
	R/Q ≤ 3	1	R/Q ≤ 3	1	R/Q ≤ 3	1	R/Q ≤ 3	1	R/Q ≤ 3	1
	R/S ≤ 3		R/S ≤ 2		R/S ≤ 2		R/S ≤ 3		R/S ≤ 3	
	R ≤ 0.6 mV		R ≤ 0.6 mV		R ≤ 0.6 mV		R ≤ 0.6 mV		R ≤ 0.6 mV	
	NtchInit40		NtchInit40		NtchInit40		NtchInit40		NtchInit40	
Total	Points		Points		Points		Points		Points	

Lead	LBBB Critera	Pts
I	any Q	1
	R/Q ≤ 1	2
	R/S ≤ 1	
	R/Q ≤ 1.5	1
	R/S ≤ 1.5	
II	Q ≥ 40 ms	2
	Q ≥ 30 ms	1
	R/Q ≤ 0.5	1
	R/S ≤ 0.5	
aVL	Q ≥ 50 ms	2
	Q ≥ 40 ms	1
	R/S ≤ 0.5	2
	R/Q ≤ 0.5	
	R/S ≤ 1	1
	R/Q ≤ 1	
aVF	Q ≥ 50 ms	2
	Q ≥ 40 ms	1
	R/Q ≤ 0.5	1
	R/S ≤ 0.5	
V1 Ant.***	NchInit40	1
	R ≥ 0.3 mV	2
	R ≥ 30 ms	
	R ≥ 0.2 mV	1
	R ≥ 20 ms	
V1 Post	S/S' ≥ 2.0	3
	S/S' ≥ 1.5	2
	S/S' ≥ 1.25	1
V2 Ant.***	NchInit40	1
	R ≥ 0.4 mV	2
	R ≥ 30 ms	
	R ≥ 0.3 mV	1
	R ≥ 20 ms	
V2 Post	S/S' ≥ 2.5	3
	S/S' ≥ 2.0	2
	S/S' ≥ 1.5	1
V5	any Q	1
	R/R' ≥ 2	2
	R/R' ≥ 1	1
	R/S ≤ 2	
	R ≤ 0.5 mV	1
V6	Q ≥ 20 ms	1
	R/R' ≥ 2	2
	R/R' ≥ 1	1
	R/S ≤ 2	
	R ≤ 0.6 mV	1
Total	Points	

%LV infarct _____
(3 *#pts)

* (for LVH) if ≥4 other points in leads I, aVL, V4, V5 or V6 then count QS in V1-V3

** (RAO) if P positive amp in V1≥0.1mV or aVF P ≥0.175 mV, then exclude V1-V2 Post criteria

*** (RAO) if P positive amp in V1 ≥0.1mV or aVF P ≥0.175 mV, then exclude V1-V2 R-criteria points

INFORMATION SHEET

TITLE OF THE STUDY: Myocardial scar Quantified by Sylvester score and correlation with MRI in Hypertrophic cardiomyopathy(HOCM) patients

Study number:

Participant's name: Date of Birth / Age (in years): son/daughter of _____

You have been informed that there is a marked hypertrophy of a part of your heart, which is believed to be the cause of your symptoms(Like syncope,palpitation,arrythmia). As part of diagnosis and treatment planning of your condition,Cardiac MRI is planned.That investigation is being routinely done in other patients also with similar indication or other appropriate indication.

You are being requested to participate in a study to evaluate the correlation between myocardial scar measured by Sylvester score and cardiac MRI.Participating in this study, in which only data from the investigations you have undergone for your diagnosis and treatment planning will be used, will in no way influence treatment decisions.

What is cardiac MRI and does it have any harmful effects?

Cardiac MRI is an advanced imaging technique which uses radio waves and a powerful magnet linked to a computer are used to make detailed pictures of heart. These images can show the difference between normal and abnormal tissue with anatomy and function.Post processing will be done using dedicated softwares. There is no risk of radiation exposure. This test is vital in diagnosis of your condition , its treatment planning and for follow up subsequently.

If you take part what will you have to do?

For this study, we'll be using some of the data like history,ECG and other clinical details, Imaging details (Cardiac MRI),treatment technique, outcome of the procedure, delayed follow up clinical and radiological regarding your disease and treatment which you undergo in this hospital.

No additional cost will be incurred /no additional drugs will be used and there are no additional risks as a part of the research.

Analysis of these data may or may not be useful for you later, but this is likely to give more understanding of this disease and treatment, for the benefit of future generation. You understand that strict confidentiality will be maintained.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

This study only analyzes the results of your investigation and treatment details and thus we do not expect any injury to happen to you but if you do develop any side effects or problems due to the study, these will be treated at this institute by the experienced team of medical professionals. We are unable to provide any monetary compensation, however.

Will you have to pay for the study?

The study will only analyze the results of the investigations which you will undergo in natural process of your treatment at this institute and no extra cost will be borne by you for this particular study.

What happens after the study is over?

You may or may not benefit from this study, however it may benefit other patients with similar illness.

Will your personal details be kept confidential?

The results of this study may be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask Dr Divyeshkumar Dadhania (9978822013)or email:drdivyesh@sctimst.ac.in or contact IEC member secretary (tel: 0471-2524263)

CONSENT FORM

TITLE OF THE STUDY: Myocardial scar Quantified by Sylvester score and correlation with MRI in Hypertrophic cardiomyopathy (HOCM) patients

Study number:

Participant's name: Date of Birth / Age (in years):

I_____ _____,

Son/daughter of _____ (Please tick boxes)

• Declare that I have read the above information provide to me regarding the study: 'Myocardial scar measured by Sylvester score and correlation with MRI in HOCM patients' and have clarified any doubts that I had. [ ]

• I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights. [ ]

• I also understand that study investigators will be using some of the data like history and other clinical details,ECG, Imaging details (Cardiac MRI), delayed follow up clinical and radiological regarding the disease and treatment which I undergo in hospital. [ ]

• I also understand that no additional cost will be incurred /no additional drugs will be used and there are no additional risks as a part of the research. [ ]

• I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the study. I agree to this access. [ ]

• I understand that my identity will not be revealed in any information released to third parties or published. [ ]

• I voluntarily agree to take part in this study. [ ]

• I received a copy of this signed consent form. [ ]

Name:

Signature:

Date:

Name of witness:

Relation to participant:

Date:

(Person Obtaining Consent) I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

_____ _____ Name and Signature of Person Obtaining Consent Principal Investigator.

കാര്യവിവരണപത്രം

പഠനശീർഷകം. ഹൈപ്പർട്രോഫിക് കാർഡിയോമയോപ്പതി (എച്ച്ഒസിഎം) രോഗികളിലെ എം ആർ ഐയും സിൽവെസ്റ്റർ സ്കോർ ഉപയോഗിച്ചുള്ള മയോകാർഡിയൽ തടിപ്പിന്റെ പരിമാണവുമായുള്ള (അളവ്) പാരസ്പപര്യം.

പഠനനമ്പർ

പങ്കാളിയുടെ പേര്

ജനനതീയതി/വയസ്സ് (വർഷത്തിൽ)

പുത്രൻ/പുത്രി

താങ്കളുടെ രോഗലക്ഷണങ്ങളുടെ (ബോധക്ഷയം, കിതപ്പ്, ഹൃദയമിടിപ്പിന്റെ താളവ്യത്യാസം) കാരണമെന്ന് വിശ്വസിക്കപ്പെടുന്ന പ്രകടമായി ഹൈപ്പർട്രോഫി ഹൃദയത്തിലൊരു ഭാഗത്ത് ഉണ്ടെന്ന് താങ്കളെ അറിയിച്ചിട്ടുണ്ട്. താങ്കളുടെ അവസ്ഥയുടെ രോഗനിർണ്ണയത്തിനും ചികിത്സ ആസൂത്രണം ചെയ്യാനുമായി ഹൃദയത്തിന്റെ എംആർഐ ഉദ്ദേശിക്കുന്നു. സമാനമായ സൂചനകളോ മറ്റ് അനുയോജ്യമായ സൂചനകളോ ഉള്ള മറ്റ് രോഗികളിലും ഈ പരിശോധന പതിവായി ചെയ്യാറുണ്ട്.
സിൽവെസ്റ്റർ സ്കോർ ഉപയോഗിച്ചുള്ള മയോകാർഡിയൽ തടിപ്പിന്റെ അളവും കാർഡിയാക് എംആർഐയും തമ്മിലുള്ള പാരസ്പര്യം അപഗ്രഥിക്കുന്ന ഈ പഠനത്തിൽ പങ്കെടുക്കുവാൻ താങ്കളോടഭ്യർത്ഥിക്കുന്നു. താങ്കൾ രോഗനിർണ്ണയത്തിനായി വിധേയമായ പരിശോധനകളുടെയും ആസൂത്രണം ചെയ്ത ചികിത്സയുടെയും വിവരങ്ങൾ മാത്രമാണ് ഉപയോഗിക്കുന്നത് എന്നതിനാൽ ഒരുവിധത്തിലും താങ്കളുടെ ചികിത്സാതീരുമാനങ്ങളെ പഠനം സ്വാധീനിക്കില്ല.

എന്താണ് കാർഡിയാക് എംആർഐ അഥവാ ഇത് ചെയ്യുന്നത് വഴി എന്തെങ്കിലും പ്രത്യാഘാതങ്ങൾ ഉണ്ടോ

കാർഡിയാക് എംആർഐ ഒരു നൂതന സാങ്കേതിക വിദ്യ വഴി ഹൃദയ പേശികളുടെ പ്രവർത്തന തകരാറുകൾ കണ്ടുപിടിക്കുന്ന യന്ത്രമാണ്. അതിശക്തമായ കാന്തിക മണ്ഡലം ഉപയോഗിച്ചുകൊണ്ട് കമ്പ്യൂട്ടറിന്റെ സഹായത്തോടുകൂടി ഹൃദയത്തിന്റെ ശരിയായ ഘടനയുടെ വ്യക്തമായ പ്രവർത്തനം പകർത്തിയെടുക്കുന്ന ഒരു സ്കാനിംഗ് രീതിയാണ് കാർഡിയാക് എംആർഐ. കമ്പ്യൂട്ടർ സോഫ്റ്റ്വെയർ സഹായത്തോടുകൂടി പകർത്തിയെടുക്കുന്ന ഈ ചിത്രങ്ങൾ ഹൃദയത്തിന്റെ സ്വാഭാവികവും അസ്വാഭാവികവുമായ സിരകളുടെയും ശരീരഘടനയുടെയും പ്രവർത്തനം മനസ്സിലാക്കാൻ കഴിയുന്നു. മറ്റു സ്കാനിംഗുകൾ പോലെ ശരീരത്തിന് ഈ സ്കാനിംഗ് കൊണ്ട് യാതൊരു ദോഷവുമില്ല. ഈ പരിശോധന താങ്കളുടെ ശരിയായ അസുഖം കണ്ടുപിടിക്കുന്നതിനും അതിന് ശേഷം ചികിത്സ തുടങ്ങുന്നതിനും തുടർചികിത്സ തീരുമാനിക്കാനും അത്യന്താപേക്ഷിതമാണ്.

ഇതിൽ പങ്കെടുത്താൽ താങ്കൾ എന്താണ് ചെയ്യേണ്ടത്

ഈ പഠനത്തിൽ താങ്കൾ പങ്കാളിയായാൽ ആശുപത്രിയിൽ താങ്കളുടെ രോഗത്തിന്റെ രേഖകൾ ഇസിജി, മറ്റു ചികിത്സാ സംബന്ധമായ വിവരങ്ങൾ, സ്കാനിംഗ് ഫിലിമുകൾ (കാർഡിയാക് എംആർഐ) ചികിത്സാ രീതികൾ ചികിത്സക്കു ശേഷമുള്ള റിപ്പോർട്ട്. തുടർചികിത്സ സംബന്ധിച്ചുള്ള താങ്കളുടെ അസുഖത്തിന്റെ രേഖകളുടേയും ചികിത്സയുടെയും വിവരങ്ങൾ നൽകേണ്ടതായി വന്നേക്കും.

ഈ പഠന പ്രവർത്തനത്തിൽ പങ്കാളിയാകുന്നതു വഴി താങ്കൾക്ക് അധിക പണമൊന്നും അടക്കേണ്ടതില്ല. അതുപോലെ അധികം മരുന്ന് ഉപയോഗിക്കുകയോ മറ്റ് അപകടമോ ഉണ്ടായിരിക്കുന്നതല്ല.

ഈ പഠനപ്രവർത്തനത്തിന്റെ ഭാഗമായി ശേഖരിക്കപ്പെടുന്ന വിവരങ്ങൾ ചിലപ്പോൾ താങ്കൾക്ക് പിന്നീട് ഉപകാരപ്പെട്ടേക്കാം. അതുപോലെ ഈ വിവരങ്ങൾ വരും തലമുറക്ക് കൂടുതലായി ഈ അസുഖത്തിനും ചികിത്സക്കും ഉപകാരപ്പെട്ടാക്കാം. താങ്കൾ നൽകുന്ന ഈ വിവരങ്ങൾ തീർച്ചയായും വളരെ രഹസ്യാമായി സൂക്ഷിക്കുന്നതായിരിക്കുമെന്ന് നിങ്ങൾ മനസ്സിലാക്കുക.

ഈ പഠനപ്രവർത്തനത്തിൽ പങ്കെടുത്താൽ ഇതിൻനിന്നും പിൻമാറാൻ സാധിക്കുമോ

ഈ പഠനപ്രവർത്തനത്തിൽ താങ്കുടെ പങ്കാളിത്തം പൂർണ്ണമായും സ്വമേധയാലും നിയന്ത്രതവുമാണ്. ഇതിൻനിന്ന് എപ്പോൾ വേണമെങ്കിലും താങ്കളുടെ സമ്മതം പിൻവലിക്കാനാകുന്നതുമാണ്. അഥവാ അങ്ങനെ ചെയ്താലും ഈ ആശുപത്രിയിൽ താങ്കൾക്ക് സാധാരണ ഗതിയിൽ ലഭിക്കുന്ന ചികിത്സയ്ക്ക് യാതൊരു രിതിയിലുള്ള തടസ്സങ്ങളും ഉണ്ടാവുകയില്ല.

ഈ പഠനത്തിന്റെ ഭാഗമായി എന്തെങ്കിലും അപകടം സംഭവിക്കുകയാണെങ്കിൽ എന്തു സംഭവിക്കും

ഈ പഠന പ്രവർത്തനം താങ്കളുടെ പരിശോധന റിപ്പോർട്ടുകളും ചികിത്സാ വിവരങ്ങളും വിശകലനം ചെയ്യുക മാത്രമാണ് ചെയ്യുന്നത്. ഇതുമൂലം താങ്കൾക്ക് യാതൊരു തരത്തിലുള്ള അപകടമോ ബുദ്ധിമുട്ടോ ഉണ്ടാവാനുള്ള സാദ്ധ്യത തീരെയില്ല. അഥവാ ഇതിന്റെ ഭാഗമായിഎന്തെങ്കിലും ബുദ്ധിമുട്ട് ഉണ്ടാവുകയാണെങ്കിൽ അത് ഈ ആശുപത്രിയിലെ അനുഭവജ്ഞരായ ഡോക്ടർമാർ ചികിത്സിക്കുന്നതായിരിക്കും. ഇതിന്റെ ഭാഗമായി സാമ്പത്തികപരമായ യാതൊരു നഷ്ടപരിഹാരങ്ങളും നൽകുന്നതല്ല.

താങ്കൾ ഈ പഠനത്തിനായി പണം അടക്കേണ്ടതുണ്ടോ

ഈ പഠനത്തിനായി സാധാരണ താങ്കൾ ഈ ആശുപത്രിയിൽ ചെയ്യുന്ന വൈദ്യപരിശോധനയുടെ റിപ്പോർട്ടുകൾ മാത്രമാണ് പരിശോധിക്കുന്നത്. ഇതിനായി താങ്കൾ അധിക പണമമൊന്നും അടക്കേണ്ടതായി വരുന്നില്ല.

ഈ പഠനം കഴിഞ്ഞാൽ എന്താണ് സംഭവിക്കുക

ഈ പഠനത്തിൽ താങ്കൾ പങ്കാളിയാവുന്നത് വഴി ചിലപ്പോൾ ഇതിന്റെ ഗുണം നിങ്ങൾക്ക് കിട്ടിയെന്നോ കിട്ടിയില്ല എന്നോ വരാം. എന്നിരുന്നാലും ഇതുപോലെ സമാനമായ അസുഖമുള്ള രോഗികൾക്ക് ഇതിന്റെ ഗുണം ചിലപ്പോൾ കിട്ടിയെന്നു വരാം.

താങ്കളുടെവ്യക്തിപരമായ വിവരങ്ങൾ രഹസ്യമായി സൂക്ഷിക്കുമോ

താങ്കൾ ഈ പഠനത്തിന്റെ പങ്കാളിയായാൽ ഈ പഠനത്തിലൂടെ ശേഖരിച്ച വിവരങ്ങൾ വൈദ്യ പ്രസിദ്ധീകരങ്ങളിൽ ഉൾപ്പെടുത്തുന്നതാണ്. എന്നാൽ പേര് വിവരങ്ങൾ ഒന്നും തന്നെ ഉൾപ്പെടു ത്തുന്നതല്ല. എന്നിരുന്നാലും താങ്കളുടെ ചികിത്സാരേഖകൾ പഠനത്തിലേർപ്പെട്ടിരിക്കുന്ന ആളുകൾ താങ്കളുടെ അനുവാദമില്ലാതെ തന്നെ വിലയിരിത്തുന്നതായിരിക്കും

തുടർന്നുള്ള അന്വേഷണങ്ങൾക്കും കൂടുതൽ വിവരങ്ങൾക്കും ബന്ധപ്പെടുക

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സമ്മതപത്രം

പഠനത്തിന്റെ പേര്. ഹൈപ്പർട്രോഫിക് കാർഡിയോമയോപ്പതി (എച്ച്ഒസിഎം) രോഗികളിലെ എം ആർഐയും സിൽവെസ്റ്റർ സ്കോർ ഉപയോഗിച്ചുള്ള മയോകാർഡിയൽ തടിപ്പിന്റ പരിമാണവുമായുള്ള (അളവ്) പാരസ്പപര്യം.

പഠനത്തിന്റെ നമ്പർ

പങ്കെടുക്കുന്ന ആളിന്റെ പേര്

ജനനതിയതി

ഞാൻ .....മകൻ/മകൾ

താഴെ കൊടുത്തിരിക്കുന്ന ബോക്സ് ടിക് ചെയ്യുക

മുകളിൽ പറഞ്ഞിരിക്കുന്ന പഠനത്തെപ്പറ്റി ഞാൻ വിവരങ്ങൾ വായിച്ച് മനസ്സിലാക്കുകയും എനിക്കുണ്ടായ എല്ലാ സംശയങ്ങളും നിവാരണം നടത്തിയിട്ടുണ്ട് എന്ന് ഞാൻ സമ്മതിക്കുന്നു [ ]

ഈ പഠനത്തിൽ പങ്കെടുക്കാനുള്ള എന്റെ തീരുമാനം സ്വമേധയായായതും നിയമപരമായ എല്ലാ അവകാശങ്ങളോടും കൂടി തന്നെ എന്റെ ചികിതസയെ ബാധിക്കാതെ ഏത് സമയത്തും എന്റെ സമ്മതം പിൻവലിക്കാവുന്നതാണെന്നും ഞാൻ മനസ്സിലാക്കുന്നു [ ]
ഞാൻ പഠനത്തിൻനിന്നും പിൻമാറിയാലും എന്റെ അസുഖവിവരങ്ങൾ പഠനത്തിലേർപ്പെട്ടിരിക്കുന്ന സ്റ്റാഫുകൾക്കും, സ്ഥാപനത്തിന്റെ എത്തിക്സ് കമ്മറ്റിക്കും എന്റെ അധികാരമില്ലാതെ തന്നെ പരിശോധിക്കാനുള്ള അധികാരമുണ്ടായിരിക്കുമെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു [ ]

എന്റെ വ്യക്തിപരമായ കാര്യങ്ങൾ മറ്റൊരാൾക്കും കൈമാറ്റം ചെയ്യപ്പെടുകയില്ല എന്നും ഞാൻ മനസ്സിലാക്കുന്നു [ ]

ഈ പഠന പ്രവർത്തനം കഴിയുമ്പോൾ എന്റെ വ്യക്തിപരമായ കാര്യങ്ങൾ പ്രസിദ്ധീകരണങ്ങളിലോ മറ്റൊരാളിലേയ്ക്കോ കൈമാറില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു [ ]

ഞാൻ ഈ പഠനത്തിൽ സ്വമേധയാൽ പങ്കാളിയാകുന്നു [ ]

ഒപ്പിട്ട ഈ സമ്മത പത്രത്തിന്റെ ഒരു കോപ്പി ഞാൻ കൈപ്പറ്റിയിരിക്കുന്നു [ ]

പേര്

ഒപ്പ്

തിയതി

സാക്ഷിയുടെ പേര്

പങ്കെടുക്കുന്ന ആളുമായുള്ള ബന്ധം

തിയതി

വൈദ്യഗവേഷണ പഠനത്തിന്റെ ആവശ്യകതയെപ്പറ്റി അറിയിച്ചുകൊണ്ടുള്ള ഈ സമ്മതപത്രം തൃപ്തികരമാണെന്ന് ഞാൻ വിലയിരുത്തുന്നു. ഗവേഷണപഠനത്തെപ്പറ്റി ഈ സമ്മതപത്രത്തിലുൾപ്പെട്ടിരിക്കുന്ന കാര്യങ്ങൾ പങ്കെടുക്കുന്ന വ്യക്തിയോട് വിശദീകരിച്ചിട്ടുണ്ട്. ഉണ്ടാകാനിടയുള്ള, അപകടങ്ങളെപ്പറ്റിയും, പ്രത്യാഘാതങ്ങളെപ്പറ്റിയും ഞാൻ വിശദമായി പ്രതിപാദിച്ചിട്ടുണ്ട്. തുടർന്നും പങ്കെടുക്കുന്ന വ്യക്തിയെ ചോദ്യങ്ങളും സംശയങ്ങളും ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും അവയ്ക്കെല്ലാം ഉത്തരം നൽകുകയും ചെയ്തിട്ടുണ്ട്.

സമ്മതപത്രം ഒപ്പിട്ടുവാങ്ങിയ ആളുടെ പേരും ഒപ്പും.

Proforma

Sex:
Age:
Clinical diagnosis:
Family history:
DM:
HTN:
DLP:
Chief complaints:
Holter NSVT burden:
Pro BNP:
Syncope:
Echo: EF-

Sylvester score:
Max LV wall thickness
Myocardial Mass: Absolute-
Index-
LVEF:
LGE scar:5SD-
FWHM-

IEC Approval

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
(An Institute of National Importance under Govt. of India)
Grams : Chitramet, Phone : +91-471-2443152, Fax : +91-471-2550728 / 2446433, E-mail : sct@sctimst.ac.in, Website : www.sctimst.ac.in

Institutional Ethics Committee
(IEC Regn No. ECR/189/Inst/KL/2013/RR-16)

SCT/IEC/1408/JULY-2019 22.08.2019

Dr. Divyeshkumar Dadhania
Senior Resident, Department of IS & IR
SCTIMST, Thiruvananthapuram

Dear Dr. Divyeshkumar Dadhania,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "MYOCARDIAL SCAR QUANTIFIED BY SELVESTER SCORE AND CORRELATION WITH MRI IN HYPERTROPHIC CARDIOMYOPATHY (HCM) PATIENTS (IEC/1408)" on 26th July, 2019.

The following documents were reviewed:

Original submission

1. *Covering Letter addressed to the Chairperson, IEC, SCTIMST dated 27.06.2019 s with checklist*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Proforma*
6. *Information Sheet and Consent Form in English and Malayalam*
7. *CV of Principal Investigator and Co-Principal Investigators*

Revised submission

1. *Covering Letter addressed to the Member Secretary, IEC, SCTIMST dated 12.08.2019 s with checklist*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Proforma*
6. *Information Sheet and Consent Form in English and Malayalam*
7. *CV of Principal Investigator and Co-Principal Investigators*

The following members of the Ethics Committee were present at the meeting held on 26th July, 2019 at Noshir H Wadia Conference Hall, AMCHSS, SCTIMST

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. Harikrishnan S	MD, DM (Cardiology) DNB (Cardiology)	Male	Clinician	Yes
2.	Dr. Kala Kesavan. P	MBBS, MD	Female	Basic Medical Scientist	No
3.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
4.	Dr. Christina George	MD Psychiatry	Female	Clinician	No
5.	Dr. Mala Ramanathan	PhD	Female	Social Scientist (Member Secretary)	Yes

IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:
The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Mala Ramanathan
Member Secretary, IEC